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PATENT
Attorney Docket No. 1142.0068-00

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPROVED
APR 12 2000
Marietta Joyce
FOR THE COMMISSIONER OF PATENTS

In re U.S. Patent No.: 4,626,538

Inventors: Dusza et al.

Issue Date: December 2, 1986

Assigned: American Cyanamid Company

For: [7-(3-DISUBSTITUTED AMINO)PHENYL] PYRAZOLO[1,5-A]PYRIMIDINES

Attn: Office of Petitions
Crystal Plaza 4-3C23

CERTIFICATE
JUN 22 1999
OF CORRECTION

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

REQUEST FOR CERTIFICATE OF CORRECTION UNDER 35 U.S.C. § 254, OR IN THE ALTERNATIVE, A PETITION UNDER 37 C.F.R. § 1.182 TO RESET THE EFFECT OF A TERMINAL DISCLAIMER IN ACCORDANCE WITH 35 U.S.C. § 154(c)(1)

American Cyanamid Company is the owner of the above-identified patent by virtue of an Assignment recorded in the U.S. Patent and Trademark Office (PTO) on May 13, 1985 at Reel 4406, Frame 0769. The Commissioner is requested to issue a Certificate of Correction or take other appropriate action to indicate a portion of the term of U.S. Patent No. 4,626,538 subsequent to the expiration date of U.S. Patent No. 4,521,422 has been disclaimed.

A power of attorney and statement under 37 C.F.R. § 3.73(b) is attached (Exhibit A).

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Although no fee is required to consider and grant a Certificate of Correction under 35 U.S.C. § 254, any fees necessary for consideration of this request should be charged to Deposit Account No. 06-0916.

I. Grant of U.S. Patent No. 4,626,538

U.S. Patent 4,626,538 (Exhibit B) was granted on December 2, 1986 on Application Serial No. 732,986 filed May 13, 1985. The 1985 application is a continuation-in-part of Application Serial No. 612,812 filed May 24, 1984, now U.S. Patent No. 4,521,422 (Exhibit C), which in turn is a continuation-in-part of Application Serial No. 506,966 filed June 23, 1983, now abandoned.

In an Office Action mailed November 22, 1985 (Exhibit D), in Serial No. 732,986, the PTO rejected claims under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-31 of U.S. Patent No. 4,521,422. Claims were also provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-14 and 18 of copending Application Serial No. 732,985. Applicants timely responded to the double patenting rejections by filing a terminal disclaimer (Exhibit E) pursuant to 35 U.S.C. § 253 and 37 C.F.R. § 1.321(b). In pertinent part, the terminal disclaimer contained the following statement:

> Your petitioner, AMERICAN CYANAMID COMPANY, hereby disclaims the terminal part of any patent granted on the above-identified application which would extend beyond June 3, 2002, and hereby agrees that any patent so granted on the above-identified application shall be enforceable only for and during such period that the legal title to said patent shall be the same as the legal title to United States Letters Patent No. 4,521,422 and to any patent which might issue on application Serial No. 732,985; this agreement to run with any patent granted on the above-identified application and to be binding upon the grantee, its successors or assigns.

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In remarks accompanying the response filed April 23, 1986 (Exhibit F) to the PTO action mailed November 22, 1985, applicants indicated that the terminal disclaimer was being filed to overcome the double patenting rejections. The text of the remarks in that response is as follows:

> Claims 1-14 and 18 are rejected as double patenting of the obviousness type over U.S. Patent No. 4,521,422 and provisionally rejected as double patenting of the obviousness type over their copending Application Serial No. 732,985. To overcome these rejections, pursuant to 37 C.F.R. § 1.321(b), Applicants are submitting herewith Assignee's disclaimer of the term of any patent granted on the above-identified Application which would extend beyond the expiration date of U.S. Patent No. 4,521,422 (June 3, 2002) and Assignee's acknowledgment that any patent granted on said Application would be enforceable only for such time as its legal title is identical to the legal title of U.S. Patent No. 4,521,422 and to any patent which might issue on Application Serial No. 732,985.
>
> In view of the terminal disclaimer, Claims 1-14 and 18 are patentable over U.S. Patent No. 4,521,422 and any patent issuing on Application Serial No. 732,985.

(Emphasis added.)

Consideration of the amendment filed April 23, 1986, resulted in the issuance of a Notice of Allowance and Issue Fee Due on June 26, 1986. Following timely payment of the issue fee, the patent was granted on December 2, 1986.

The face of U.S. Patent 4,626,538 contains the following notice:[1]

> A portion of the term of this patent subsequent to June 3, 2002 has been disclaimed.

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[1] It was standard PTO practice in 1986 to identify a specific date in the terminal disclaimer data field on the face of the patent grant. This practice was followed regardless of the form or specific words used in the terminal disclaimer filed under 35 U.S.C. § 253.

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As noted in the remarks section of the amendment filed April 23, 1986, the date corresponds to the then perceived expiration date of U.S. Patent No. 4,521,422, and is the date contained in the terminal disclaimer filed April 23, 1986.

II. Uruguay Round Agreement Act

The Uruguay Round Agreement Act, Pub. L. No. 103-465, 108 Stat. 4809 (1994) (URAA), was enacted on December 8,1994. Among the changes introduced by the URAA were those directed to the term of a patent in the United States. Section 532 of the URAA (Exhibit G) introduced a 20-year patent term. The purpose of the patent term provisions of the URAA was to harmonize the term provision of United States patent law with that of our trading partners which grant a patent term of 20 years from the date of filing of a patent application. Merck v. Kessler, 80 F.3d 1543, 1547, 38 USPQ2d 1347, 1349 (Fed. Cir. 1996).

The patent term provisions adopted in the URAA affect not only the term of patents issued on applications filed after the effective date of enactment of the term provisions (June 8, 1995), but also affect certain patents which were issued and in force on the date of enactment, and patents issued on those pending applications which were filed prior to June 8, 1995. Patents in force on June 8, 1995, are entitled under the patent term resetting provisions of 35 U.S.C. § 154(c)(1) to the longer of the 17-year term from grant of the patent or a 20-year from filing term, subject to any terminal disclaimers.

The Administration and Congress provided explicit guidance on how the term of a patent in force subject to a terminal disclaimer would be affected by the patent term resetting provisions of the URAA. Specifically, Congress approved a Statement of Administrative Action (Exhibit H) that was proposed to implement the agreements that

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were submitted to the Congress on September 27, 1994.[2] As noted at the beginning of the Statement of Administrative Action:

> . . . this Statement represents an authoritative expression by the Administration concerning its views regarding the interpretation and application of the Uruguay Round agreements, both for the purposes of U.S. international obligations and domestic law. Furthermore, the Administration understands that it is the expectation of the Congress that future Administrations will observe and apply the interpretations and commitments set out in this Statement. Moreover, since this Statement will be approved by the Congress at the time it implements the Uruguay Round agreements, the interpretations of those agreements included in this Statement carry particular authority.

1994 U.S.C.C.A.N. 4040.

The portion of the Statement of Administrative Action relevant to the patent term resetting provisions of § 154(c)(1) provides as follows:

> . . . . section 532(a) of the implementing bill amends section 154 to provide that the term of a patent in force on, or that results from an application filed before, the date that is six months after the date of enactment of the Uruguay Round Agreement Act will be the greater of 17 years from the date of patent grant or 20 years from the date of filing of the application leading to the patent. A patent whose term has been disclaimed under section 253 of Title 35 due to another patent on an invention that is not patentably distinct from but was owned by or subject to an obligation of assignment to the same person shall expire on the date of the other patent. A patent whose term has been disclaimed under section 253 of Title 35 independent of another patent shall be reduced by the length of the originally disclaimed period.

1994 U.S.C.C.A.N. 4296 (emphasis added).

It is clear that the Administrative Action Statement addresses two situations where a terminal disclaimer would affect the term of a patent in force. First, where the terminal

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[2] URAA, Section 101(a)(2) of Title 1, Subtitle A, 108 Stat. 4814 (Exhibit I).

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disclaimer was filed to overcome a double patenting rejection, the Administrative Action Statement clearly indicates that the effect of the patent term resetting provisions of § 154(c)(1) is that the patent containing the terminal disclaimer "shall expire on the date of the other patent." In the second situation, the terminal disclaimer has been filed independent of another patent, such as a terminal disclaimer filed in conjunction with a petition to revive an abandoned application under 37 C.F.R. § 1.137. In that case, the term of the patent is still extended, but the length of the extension is "reduced by the length of the originally disclaimed period."

The patent term resetting provisions of § 154(c)(1) occurred by operation of law. They did not require the adoption of implementing regulations by the Commissioner or any action on the part of affected patentees or patent applicants. This request for a certificate of correction addresses the impact of the URAA on the patent term of U.S. Patent No. 4,626,538.

III. Action Requested

The Commissioner is requested to issue a certificate of correction under 35 U.S.C. § 254 to indicate on the face of the patent that the portion of the term of this patent subsequent to the expiration date of U.S. Patent No. 4,521,422 has been disclaimed.

The patent owner recognizes that the terminal disclaimer as filed disclaimed the term of the '538 patent beyond the expiration date of the '422 patent which was considered to be June 3, 2002 - 17 years from the date of grant. Arguably, the '538 patent was correct as issued, but now contains an error by virtue of the operation of the patent term resetting provisions of the URAA contained in § 154(c)(1). In the event the Commissioner considers the issuance of a certificate of correction under § 254 is not the

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appropriate remedial procedure in these circumstances, relief is requested under 37 C.F.R. § 1.182.

The term of each patent issued by the PTO is important. The term of U.S. Patent No. 4,626,538 is particularly important since this patent claims a product that is currently undergoing premarket regulatory review at the Food and Drug Administration (FDA). This patent is a likely candidate for patent term extension under 35 U.S.C. § 156 once the product is approved by the FDA. The original expiration date of U.S. Patent No. 4,626,538 will have a significant impact on the expiration date of the patent term as extended under 35 U.S.C. § 156.

IV. Arguments

United States Patent No. 4,521,422 was issued on June 4, 1985 for a term of 17 years. Accordingly, the anticipated expiration date of the '422 patent at the time of grant was June 3, 2002. All maintenance fees have been paid on the '422 patent.

During the prosecution of the application that matured into U.S. Patent No. 4,626,538, applicants filed a terminal disclaimer to overcome a double patenting rejection based on the '422 patent. A terminal disclaimer was filed under 35 U.S.C. § 253 and 37 C.F.R. § 1.321(b). It is clear from the terminal disclaimer itself that the disclaimer was considered to be linked to the then perceived expiration date of the '422 patent by the specific recitation of the perceived expiration date of the '422 patent (June 3, 2002), and by the averment that any patent granted on the subject application would be enforceable only for and during such period that the legal title to the patents, including the '422 patent, shall be the same. The prosecution history of the '538 patent expressly states that the terminal disclaimer was submitted to disclaim the term of the patent "which would extend

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beyond the expiration date of U.S. Patent No. 4,521,422 (June 3, 2002)," along with the averment regarding common ownership (page 2 of amendment filed April 23, 1986). The '538 patent as granted on December 2, 1986, contained the notice that "The portion of the term of this patent subsequent to June 3, 2002 has been disclaimed." All maintenance fees have been paid on the '538 patent.

Under the URAA, the patent term of the '422 patent was reset to expire 20 years from the date of the original filing - i.e. June 23, 2003. The '422 patent issued on an application that was a continuation-in-part of an application filed June 23, 1983. The '422 patent was a patent in force on June 8, 1995, and thus entitled to the provisions of § 154(c)(1).

Similarly, the '538 patent is entitled to the patent term resetting provisions of § 154(c)(1) because it was a patent in force on June 8, 1995. As noted above, the patent term resetting provisions of § 154(c)(1) are subject to any terminal disclaimers. The Administrative Action Statement accompanying the URAA makes clear that when a patent has been terminally disclaimed to overcome a double patenting rejection over a first patent, the patent term resetting provisions of § 154(c)(1) by operation of law result in the extension of patent term of the disclaimed patent to the date of expiration of the first patent. The consequences described in the Administrative Action Statement are clear, mandatory ("shall expire"), and are not linked to any form or wording contained in the terminal disclaimer. Accordingly, it is respectfully submitted that the patent term resetting provisions of § 154(c)(1) result, by operation of law, in resetting the expiration date of the '538 patent to the reset expiration date of the '422 patent - i.e. June 23, 2003.

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It is clear from the terminal disclaimer and prosecution history of the '538 patent that the terminal disclaimer was filed under 35 U.S.C. § 253 to overcome a double patenting rejection. It is equally clear that the '538 patent was a patent in force on June 8, 1995, and thus entitled to the benefits of the patent term resetting provisions of § 154(c)(1). The face of the '538 patent now contains an error which can be corrected by Certificate of Correction under § 254. An appropriate Certificate of Correction is attached (Exhibit J).

We are aware that the PTO has addressed the issue of the effect of § 154(c)(1) on patents containing a terminal disclaimer. See e.g., decisions rendered in U.S. Patent Nos. 4,346,116 (Exhibit K) and 4,654,073 (Exhibit L). It is not apparent in either of these decisions whether the PTO considered the effect of the authoritative expression of Administration and Congressional intent contained in the Statement of Administrative Action. We think there is a compelling argument for correction in this case based on the Statement of Administrative Action.

Even if the Statement of Administrative Action was considered in the prior decisions, correction in this case is consistent with past PTO action on this issue. Specifically, the file history, including the terminal disclaimer, in U.S. Patent No. 4,654,073 indicated that the terminal part of the patent was being disclaimed "beyond the expiration date of United States Patent No. 4,422,864 (expiration date December 27, 2000)." The term of the '864 patent was reset to expire on May 20, 2002, by operation of § 154(c)(1). The PTO issued a Certificate of Correction under 35 U.S.C. § 254 to resolve an alleged ambiguity that was present in the terminal disclaimer that allegedly made reference to two

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(2) dates: December 27, 2000 (the original expiration date), and May 20, 2002 (the reset expiration date).

The '538 file history similarly makes reference, as noted above, to filing a terminal disclaimer to disclaim the term of any patent which would extend beyond "the expiration date of U.S. Patent No. 4,521,422 (June 3, 2002)." (Exhibit F) The expiration date of the '422 Patent as reset by operation of § 154(c)(1) is June 23, 2003. Since the file history of the '538 patent raises the same alleged ambiguity as the file history of the '864 patent, a Certificate of Correction should be issued in the '538 patent.

In the PTO decision involving U.S. Patent No. 4,346,116, a request to rescind the terminal disclaimer under 37 C.F.R. § 1.182 was denied. The request and file history in the '538 patent are dissimilar in several respects from those in the '116 patent. First, no request is being made in the '538 patent to rescind a terminal disclaimer. Second, the file history in the '538 patent makes clear that the terminal disclaimer is linked to the "expiration date of U.S. Patent No. 4,521,422," whereas the file history in the '116 patent does not contain such an explicit statement. Thus, the decision in the '116 patent is not controlling in the circumstances in the present case.

In addition, the arguments relied on by the PTO to support the decision in the '116 patent are not applicable to the facts in this case. For example, the decision in In re Jentoft, 392 F.2d 633, 639, n.6, 157 USPQ 363, 368, n.6 (CCPA 1968), which characterized the filing of an unnecessary terminal disclaimer as "an unhappy circumstance," is not applicable to the facts in this case since the patentee is not alleging that a terminal disclaimer was unnecessary. On the contrary, the issue presented in this case is the impact of § 154(c)(1) on a patent that contains a terminal disclaimer.

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In its decision in the '116 patent, the PTO also relied on a public policy against restoring to the patentee something that has been freely dedicated to the public. This policy as allegedly supported by Altoona Publix Theatres v. American Tri-Ergon Corp., 294 U.S. 477, 24 USPQ 308 (1935). This decision is not, however, applicable to the facts in this case where rights accrue to the patentee by operation of law. Just as the PTO has granted extensions of the patent term under § 156 in patents that contain a terminal disclaimer, so too should patents containing a terminal disclaimer be entitled to the patent term resetting provisions of § 154(c)(1). Finally, there are no diligence requirements in the statute or regulations that would permit the Commissioner to raise an issue about the timeliness of filing a request for a Certificate of Correction under § 254.

For all the reasons advanced above, the patent term of U.S. Patent No. 4,626,538 was reset to expire on the reset expiration date of U.S. Patent No. 4,521,422. To deny the '538 patent the benefits of § 154(c)(1) because of the specific language used in the terminal disclaimer would be to exalt form over substance, and would be clearly contrary to explicit Administration and Congressional guidance contained in the Statement of Administrative Action. Further, when Congress intended that a patent subject to a terminal disclaimer not be entitled to a benefit introduced by the URAA, it specifically so provided. See § 154(b)(2).

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V. Conclusion

The patent term of U.S. Patent No. 4,626,538 was reset according to the provisions of § 154(c)(1) on June 8, 1995, to expire on the reset expiration date of U.S. Patent No. 4,521,422 (June 23, 2003). The patent owner requests that a Certificate of Correction be issued to correct this error on the face of the '538 patent.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

By: Charles E. Van Horn
Charles E. Van Horn
Reg. No. 40,266

Dated: June 15, 1999

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EXHIBIT A

PATENT
Atty. Docket No.: 1142.0068-00

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re U.S. Patent No. 4,626,538

Issued: December 2, 1986

To: John P. Dusza,
Andrew S. Tomcufcik,
Jay D. Albright

Assignee: American Cyanamid Company

For: [7-(3-DISUBSTITUTED AMINO)PHENYL] PYRAZOLA[1,5-A]PYRIMIDINES

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

POWER OF ATTORNEY
AND STATEMENT UNDER 37 C.F.R. § 3.73(b)

Assignee, American Cyanamid Company, being the owner of the above-identified U.S. Letters Patent, hereby grants the power of attorney to **FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER, L.L.P., Reg. No. 22,540,Douglas B. Henderson, Reg. No. 20,291; Ford F. Farabow, Jr., Reg. No. 20,630; Arthur S. Garrett, Reg. No. 20,338; Donald R. Dunner, Reg. No. 19,073; Brian G. Brunsvold, Reg. No. 22,593; Tipton D. Jennings, IV, Reg. No. 20,645; Jerry D. Voight, Reg. No. 23,020; Laurence R. Hefter, Reg. No. 20,827; Kenneth E. Payne, Reg. No. 23,098; Herbert H. Mintz, Reg. No. 26,691; C. Larry O'Rourke, Reg. No. 26,014; Albert J. Santorelli, Reg. No. 22,610; Michael C. Elmer, Reg. No. 25,857; Richard H. Smith, Reg. No. 20,609; Stephen L. Peterson, Reg. No. 26,325; John M. Romary,**

Reg. No. 26,331; Bruce C. Zotter, Reg. No. 27,680; Dennis P. O'Reilley, Reg. No. 27,932; Allen M. Sokal, Reg. No. 26,695; Robert D. Bajefsky, Reg. No. 25,387; Richard L. Stroup, Reg. No. 28,478; David W. Hill, Reg. No. 28,220; Thomas L. Irving, Reg. No. 28,619; Charles E. Lipsey, Reg. No. 28,165; Thomas W. Winland, Reg. No. 27,605; Basil J. Lewris, Reg. No. 28,818; Martin I. Fuchs, Reg. No. 28,508; E. Robert Yoches, Reg. No. 30,120; Barry W. Graham, Reg. No. 29,924; Susan Haberman Griffen, Reg. No. 30,907; Richard B. Racine, Reg. No. 30,415; Thomas H. Jenkins, Reg. No. 30,857; Robert E. Converse, Jr., Reg. No. 27,432; Clair X. Mullen, Jr., Reg. No. 20,348; Christopher P. Foley, Reg. No. 31,354; John C. Paul, Reg. No. 30,413; Roger D. Taylor, Reg. No. 28,992; David M. Kelly, Reg. No. 30,953; Kenneth J. Meyers, Reg. No. 25,146; Carol P. Einaudi, Reg. No. 32,220; Walter Y. Boyd, Jr., Reg. No. 31,738; Steven M. Anzalone, Reg. No. 32,095; Jean B. Fordis, Reg. No. 32,984; Barbara C. McCurdy, Reg. No. 32,120; James K. Hammond, Reg. No. 31,964; Richard V. Burgujian, Reg. No. 31,744; J. Michael Jakes, Reg. No. 32,824; Dirk D. Thomas, Reg. No. 32,600; Thomas W. Banks, Reg. No. 32,719; Christopher P. Isaac, Reg. No. 32,616; Bryan C. Diner, Reg. No. 32,409; M. Paul Barker, Reg. No. 32,013; Andrew Chanho Sonu, Reg. No. 33,457; David S. Forman, Reg. No. 33,694; Vincent P. Kovalick, Reg. No. 32,867; James W. Edmondson, Reg. No. 33,871; Michael R. McGurk, Reg. No. 32,045; Joann M. Neth, Reg. No. 36,363; Gerson S. Panitch, Reg. No. 33,751; Cheri M. Taylor, Reg. No. 33,216; Charles E. Van Horn, Reg. No. 40,266; Linda A. Wadler, Reg. No. 33,218; Jeffrey A. Berkowitz, Reg. No. 36,743; Michael R. Kelly, Reg. No. 33,921;

and James B. Monroe, Reg. No. 33,971; both jointly and separately to be attorneys for American Cyanamid Company with regard to A Request for Certificate of Correction under 35 U.S.C. § 254, or in the Alternative, A Petition Under 37 C.F.R. § 1.182 to Reset the Effect of a Terminal Disclaimer in Accordance with 35 U.S.C. § 154(c)(1) of U.S. Patent 4,626,538 and to transact all business in the Patent and Trademark Office connected therewith.

The inventors originally named in the above-identified Patent No. 4,626,538 have assigned their rights to American Cyanamid Company by virtue of assignment to American Cyanamid Company recorded at Reel 4406, Frames 0769.

The undersigned, whose title appears below, is empowered to sign on behalf of the assignee in this matter.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Please send all future correspondence concerning the above matter to

Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P., at the following address:

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AMERICAN CYANAMID COMPANY

Date: June 11, 1999

Egon E. Berg
Name: Egon E. Berg
Title: Assistant Secretary

EXHIBIT B

United States Patent [19]

Dusza et al.

[11] **Patent Number: 4,626,538**

[45] **Date of Patent: * Dec. 2, 1986**

[54] **[7-(3-DISUBSTITUTED AMINO)PHENYL]PYRAZOLO[1,5-A]PYRIMIDINES**

[75] Inventors: **John P. Dusza**, Nanuet, N.Y.; **Andrew S. Tomcufcik**, Old Tappan, N.J.; **Jay D. Albright**, Nanuet, N.Y.

[73] Assignee: **American Cyanamid Company**, Stamford, Conn.

[*] Notice: The portion of the term of this patent subsequent to Jun. 3, 2002 has been disclaimed.

[21] Appl. No.: **732,986**

[22] Filed: **May 13, 1985**

Related U.S. Application Data

[63] Continuation-in-part of Ser. No. 612,812, May 24, 1984, Pat. No. 4,521,422, which is a continuation-in-part of Ser. No. 506,966, Jun. 23, 1983, abandoned.

[51] **Int. Cl.**[4] **A61K 31/505; C07D 471/04**

[52] **U.S. Cl.** **514/258; 514/906; 544/281**

[58] **Field of Search** **544/281; 514/258**

[56] **References Cited**

U.S. PATENT DOCUMENTS

4,178,449	12/1979	Dusza et al.	544/281
4,236,005	11/1980	Dusza et al.	544/281
4,281,000	7/1981	Dusza et al.	544/281
4,521,422	6/1985	Dusza et al.	544/281
4,576,943	3/1986	Tomcufcik et al.	544/281

Primary Examiner—Donald G. Daus
Assistant Examiner—Stephen M. Kapner
Attorney, Agent, or Firm—Susan H. Rauch

[57] **ABSTRACT**

Novel [7-(3-disubstituted amino)phenyl]pyrazolo[1,5-a]pyrimidines useful as anxiolytic, antiepileptic and sedative-hypnotic agents as well as skeletal muscle relaxants, methods of using these compounds, compositions of matter containing them and processes for their production.

15 Claims, No Drawings

[7-(3-DISUBSTITUTED AMINO)PHENYL]PYRAZOLO[1,5-A]PYRIMIDINES

CROSS REFERENCE TO RELATED APPLICATIONS

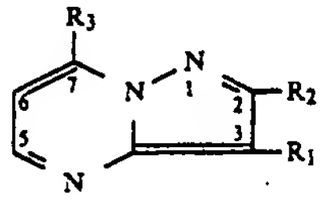
This application is a continuation-in-part of our copending application, U.S. application Ser. No. 612,812, filed May 24, 1984, now U.S. Pat. No. 4,521,422, which is a continuation-in-part of U.S. application Ser. No. 506,966, filed June 23, 1983, now abandoned.

SUMMARY OF THE INVENTION

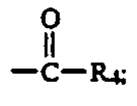
This invention relates to new organic compounds which are [7-(3-disubstituted amino)phenyl]-pyrazolo[1,5-a]pyrimidines, which are useful as anxiolytic and antiepileptic agents as well as sedative-hypnotic agents and skeletal muscle relaxants. This invention also relates to the methods of using the novel compounds, to compositions of matter containing them as the active ingredient and to processes for their production.

DETAILED DESCRIPTION OF THE INVENTION

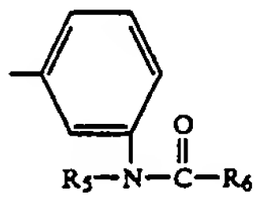
The novel compounds of this invention are represented by the following structural formula:



wherein R_1 is selected from the group consisting of: hydrogen, halogen, cyano and

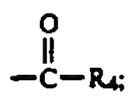


R2 is selected from the group consisting of hydrogen and alkyl(C_1-C_3); R_3 is



R_4 is selected from the group consisting of hydrogen, alkyl(C_1-C_6) and alkoxy(C_1-C_6); R_5 is selected from the group consisting of hydrogen, alkyl(C_1-C_6), alkenyl(C_2-C_6), $-CH_2C{\equiv}CH$, cycloalkyl(C_3-C_6)methyl, $-CH_2OCH_3$ and $-CH_2CH_2OCH_3$; and R_6 is selected from the group consisting of alkyl(C_1-C_6), cycloalkyl(C_3-C_6), —O—alkyl(C_1-C_6), —NH—alkyl(C_1-C_3), —N—dialkyl(C_1-C_3), $-(CH_2)_n$—O—alkyl(C_1-C_3), $-(CH_2)_n$—NH-alkyl(C_1—C_3) and $-(CH_2)_n$—N—dialkyl(C_1-C_3), where n is an integer 1 to 3 inclusive.

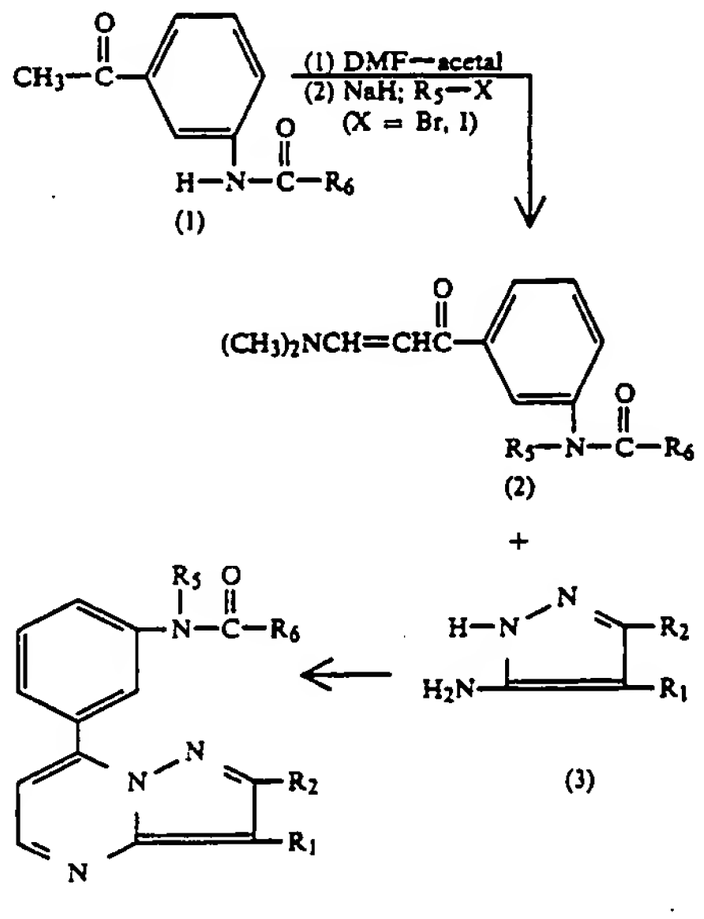
The most preferred compounds of this invention are the compounds of the above formula wherein R_1 is cyano or



R_2 is hydrogen; R_4 is alkyl(C_1-C_6); R_5 is alkyl(C_1-C_6), alkenyl(C_2-C_6) or $-CH_2{\equiv}CH$; and R_6 is alkyl(C_1-C_6), cycloalkyl(C_3-C_6) or —O —alkyl(C_1-C_6).

The instant invention is additionally concerned with the methods which employ the above-described compounds in mammals to treat anxiety or epilepsy and to induce a sedative-hypnotic effect or relax skeletal muscles, with compositions of matter containing the above-described compounds and with processes for producing the compounds.

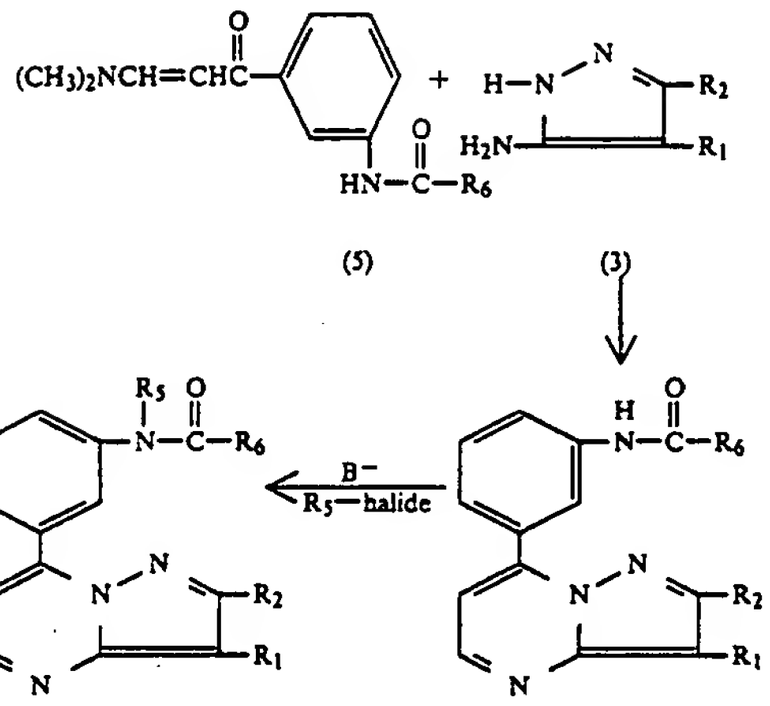
The novel compounds of this invention may be readily prepared as set forth in the following reaction scheme:



(4)

In accordance with the above reaction scheme a 1-acetylphenyl-3-amide (1), where R6 is as described above is reacted with dimethylformamide dimethylacetal at reflux giving an N-[3-[3-(dimethylamino)-1-oxo-2-propenyl[phenyl]alkanamide, which is then reacted with sodium hydride, and the anion generated is reacted with an alkyl halide, where R_5 is as described, above giving the N-[3-[3-(dimethylamino)-1-oxo-2-propenyl]-phenyl]-N-alkylalkanamide (2). This compound is than reacted with a 3-aminopyrazole (3), where R_1 and R_2 are as described above, in glacial acetic acid at reflux, giving the product (4).

Alternatively, N-[3-[3-(dialkylamino)-1-oxo-2-propenyl]phenyl]alkanamide (5) is reacted with a 3-aminopyrazole (3) to give intermediates (6) which are reacted with a base such as sodium hydride, sodium alkoxide and the like and an R_5-halide to give the products (4).



Details of the preparative scheme are fully apparent from the U.S. Pat. No. 4,521,422, which is hereby incorporated by reference.

The performance of the novel compounds of the present invention in standard tests with laboratory animals which are known to correlate well with relief of anxiety in man indicates that they possess central nervous system activity at nontoxic doses and thus are useful as anxiolytic agents. Furthermore, these compounds have been shown by biological data to be useful as antiepileptic agents, particularly in the treatment of grand mal epilepsy seizures, and as sedative-hypnotic and skeletal muscle relaxant agents.

The anti-anxiety and anticonvulsant properties of the novel compounds of the present invention have been established in a test which indicates anxiolytic and antiepileptic activity by the measure of protection they provide from convulsions resulting from the administration of pentylenetetrazole. Single or graded dose levels of the test compounds were administered orally or intraperitoneally in a 2% starch vehicle, containing 0.5% v/v polyethylene glycol and one drop of Polysorbate 80 to groups of at least 4 rats. At 30 or 60 minutes, the rats were treated intravenously with pentylenetetrazole at a dose of 23 mg/kg of body weight. This dose is estimated to cause clonic seizures in 99% of unprotected rats. It has been reported [R. T. Hill and D. H. Tedeschi, "Animal Testing and Screening Procedures in Evaluating Psychotropic Drugs" in "An Introduction to Psychopharmacology", Eds. R. R. Rech and K. E. Moore, Raven Press, New York, p. 237–288 (1971)] that there is a high degree of correlation between the ability of compounds to inhibit the seizure-inducing effect of pentylenetetrazole in rats and the effectiveness of those compounds as anxiolytic and anticonvulsive agents in higher warm-blooded animals. The results of this test on representative compounds of the present invention are shown in Table I.

TABLE I

Compound	Dose (mg/kg)	% of Rats Protected
Protection Against Clonic Seizures Caused by Pentylenetetrazole in Rats		
N—[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N—ethylpropanamide	25.0	100
N—[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N—ethylacetamide	25.0	100

TABLE I-continued

Compound	Dose (mg/kg)	% of Rats Protected
Protection Against Clonic Seizures Caused by Pentylenetetrazole in Rats		
N—[3-(3-chloropyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N—ethylacetamide	25.0	100
N—[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N—propylacetamide	6.25	100
[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]methylcarbamic acid, methyl ester	3.1	25
[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]ethylcarbamic acid, methyl ester	12.6	75
N—butyl-N—[3-(3-cyanopyrazolo[1,5-a]-pyrimidin-7-yl)phenyl]acetamide	25.0	50
[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]ethylcarbamic acid, ethyl ester	25.0	25
[3-(3-chloropyrazolo[1,5-a]pyrimidin-7-yl)phenyl]ethylcarbamic acid, ethyl ester	25.0	25
N—[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N—2-propenylacetamide	25.0	100
N—[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N—2-propynylacetamide	6.25	100
N—[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N—methylcyclobutanecarboxamide	25.0	50
N—[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N—methylcyclopropanecarboxamide	25.0	75
N—[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N—methylacetamide	25.0	75
N—[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N—methylacetamide	12.5	50
7-[3-(acetylmethylamino)phenyl]pyrazolo[1,5-a]pyrimidine-3-carboxylic acid, ethyl ester	25.0	100
N—[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N—methylpropanamide	12.5	50
N—[3-(3-cyano-2-methylpyrazolo[1,5-a]-pyrimidin-7-yl)phenyl]-N—methylpropanamide	25.0	100

Another test which has been used to assess antianxiety effects is a nonconditioned passive avoidance procedure described by J. R. Vogel, B. Beer and D. E. Clody, "A Simple and Reliable Conflict Procedure for Testing Anti-Anxiety Agents", Psychopharmacologia, 21, 1–7 (1971). A conflict situation is induced in rats by a modification of this method.

Groups of 6 native, Wistar strain rats, weighing 200–240 g each were deprived of water for 48 hours and food for 24 hours. The test compounds were administered in single or graded, oral or intraperitoneal doses, suspended in a 2% starch vehicle containing 0.5% v/v polyethylene glycol and one drop of polysorbate 80. Control animals received the vehicle alone. At 30 to 60 minutes each rat was placed in an individual plexiglass chamber. Water was available ad libitum from a tap located in the rear of the chamber. A 0.7 milliampere DC shocking current was established between the stainless steel grid floor and the tap. After 20 licks of nonshocked drinking, a shock was delivered for 2 seconds and then further shocks were delivered on a ratio of one shock for 2 seconds for every 20 licks. This was continued for a total of 3 minutes. The number of shocks taken by each rat during the 3 minute interval was recorded and compared to a control group. The test compounds are considered active if the number of shocks received by the test group is significantly higher than the control group by the Mann-Witney U test. Results of this test on

representative compounds of this invention appear in Table II.

TABLE II

Nonconditioned Passive Avoidance Test in Rats

Compound	Dose (mg/kg)	Result
N—3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N—ethylpropanamide	0.4	Active
N—3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]N—ethylacetamide	0.8	Active
N—ethyl-N—(3-pyrazolo[1,5-a]pyrimidin-7-ylphenyl)acetamide	25.0	Active
N—[3-(3-chloropyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N—ethylacetamide	3.1	Active
N—[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N—propylacetamide	1.5	Active
[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]methylcarbamic acid, methyl ester	3.1	Active
[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]ethylcarbamic acid, methyl ester	12.5	Active
[3-(3-chloropyrazolo[1,5-a]pyrimidin-7-yl)phenyl]ethylcarbamic acid, ethyl ester	25.0	Active
N—[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N—2-propenylacetamide	3.1	Active
N—[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N—2-propynylacetamide	1.5	Active
N—[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N—methylpropaneamide	6.2	Active
N—[3-(3-cyano-2-methylpyrazolo[1,5-a]-pyrimidin-7-yl)phenyl]-N—methylpropanamide	25.0	Active
7-[3-(acetylmethylamino)phenyl]pyrazolo[1,5-a]pyrimidine-3-carboxylic acid, ethyl ester	25.0	Active
N—[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N—methylacetamide	1.5	Active
N—[3-(3-chloropyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N—methylacetamide	3.1	Active
N—[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N—methylcyclobutanecarboxamide	25.0	Active

Another test utilized for the determination of anxiolytic activity is the measurement of the ability of test compounds to inhibit the binding of tritiated benzodiazepines to brain-specific receptors of warm-blooded animals. A modification of the method described by R. F. Squires, et al., Nature, 266, No. 21, p. 732 (April 1977) and H. Mohler, et al., Science, 198, p. 849 (1977) was employed.

Male albino rats (Wistar strain, weighing 150–200 g each) were obtained from Royalhart Farms. ^{3}H-Methyldiazepam (79.9 Ci/mmol) and ^{3}H-methylflunitrazepam (84.3 Ci/mmol) were obtained from New England Nuclear. The test compounds were solubilized in either dimethylformamide, acetic acid, ethanol or hydrochloric acid.

Whole cortex of rats was homogenized gently in 20 volumes of ice-cold 0.32 M sucrose, centrifuged twice at 1000 g for 10 minutes and then recentrifuged at 30,000 g for 20 minutes to produce a crude P_2-synaptosomal fraction. The P_2-fraction was either: (1) resuspended in twice the original volume in hypotonic 50 mM Tris.HCl (pH 7.4), or (2) resuspended in one-half the original volume in hypotonic 10 mM Tris.HCl (pH 7.4) and then was frozen (−20° C.) until time of use. Frozen P_2 preparations were thawed and resuspended in four times the original homogenizing volume at time of assay.

The binding assay consisted of 300 μl of the P_2-fraction suspension (0.2–0.4 mg protein), 100 μl of test drug and 100 μl of ^{3}H-diazepam (1.5 nM, final concentration) or ^{3}H-flunitrazepam (1.0 nM, final concentration) which was added to 1.5 ml of 50 mM Tris.HCl (pH 7.4). Non-specific binding controls and total binding controls received 100 μl of diazepam (3 M, final concentration) and 100 μl of deionized water, respectively, in place of the test compound. Incubation for 30 minutes proceeded in ice and was terminated by filtration, under vacuum, through Whatman GF/C glass fiber filters. The filters were washed twice with 5 ml of ice-cold 50 mM Tris.HCl (pH 7.4) and placed in scintillation vials. After drying at 50°–60° C. for 30 minutes, 10 ml of Beckman Ready-Solv ™ HP (a high performance premix scintillation cocktail, registered trademark of Beckman Instruments, Inc., Irvine, CA 92713) was added and the radioactivity determined in a scintillation counter.

Inhibition of binding was calculated by the difference between total binding and binding in the presence of test compound, divided by the total binding × 100.

The results of this test on representative compounds of the present invention are given in Table III.

TABLE III

Inhibition of the Binding of ^{3}H—Benzodiazepine to Brain-Specific Receptors of Rats

Compound	% Inhibition
N—[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N—ethylpropanamide	83
N—[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N—ethylacetamide	79
N—[3-(3-chloropyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N—ethylacetamide	97
N—[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N—propylacetamide	64
7-[3-[ethyl(1-oxopropyl)amino]phenyl]pyrazolo[1,5-a]pyrimidine-3-carboxylic acid, ethyl ester	100
[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)-phenyl]methylcarbamic acid, methyl ester	87
7-[3-[(methoxycarbonyl)methylamino]phenyl]-pyrazolo[1,5-a]pyrimidine-3-carboxylic acid, ethyl ester	98
[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)-phenyl]ethylcarbamic acid, methyl ester	55
7-[3-[ethyl(methoxycarbonyl)amino]phenyl]-pyrazolo[1,5-a]pyrimidine-3-carboxylic acid, ethyl ester	99
[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)-phenyl]methylcarbamic acid, methyl ester	41
ethyl(3-pyrazolo[1,5-a]pyrimidin-7-yl-phenyl)carbamic acid, ethyl ester	61
[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)-phenyl]ethylcarbamic acid, ethyl ester	63
[3-(3-chloropyrazolo[1,5-a]pyrimidin-7-yl)-phenyl]ethylcarbamic acid, ethyl ester	78
N—[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N—2-propenylacetamide	78
N—[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N—2-propynylacetamide	91
N—[3-(3-cyano-2-methylpyrazolo[1,5-a]pyrimidin-7-yl)phenyl]propanamide	42
N—[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N—methylpropanamide	79
N—[3-(3-cyano-2-methylpyrazolo[1,5-a]-pyrimidin-7-yl)phenyl]-N—methylpropanamide	95
N—methyl-N—(3-pyrazolo[1,5-a]pyrimidin-7-ylphenyl)acetamide	54
7-[3-(acetylmethylamino)phenyl]pyrazolo-[1,5-a]pyrimidine-3-carboxylic acid, ethyl ester	100
N—[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N—methylacetamide	73
N—[3-(3-chloropyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N—methylacetamide	71
N—[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl[-N—methylcyclobutanecarboxiamde	81
N—[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-	83

TABLE III-continued

Inhibition of the Binding of ^{3}H—Benzodiazepine to Brain-Specific Receptors of Rats	
Compound	% Inhibition
yl)phenyl]-N—methylcyclopropanecarboxamide	
7-[3-[(cyclopropylcarbonyl)methylamino]-phenylpyrazolo[1,5-a]pyrimidine-3-carboxylic acid, ethyl ester	95
7-[3-(acetylethylamino)phenyl]pyrazolo-[1,5-a]pyrimidine-3-carboxylic acid, ethyl ester	97
7-[3-(acetylamino)phenyl]pyrazolo[1,5-a]-pyrimidine-3-carboxylic acid, ethyl ester	85
7-[3-[(methoxycarbonyl)amino]phenyl]-pyrazolo[1,5-a]pyrimidine-3-carboxylic acid, ethyl ester	76
methyl(3-pyrazolo[1,5-a]pyrimidin-7-yl-phenyl)carbamic acid, methyl ester	45
7-[3-(acetylpropylamino)phenyl]pyrazolo-[1,5-a]pyrimidine-3-carboxylic acid, ethyl ester	97
[3-(3-chloropyrazolo[1,5-a]pyrimidin-7-yl)phenyl]methylcarbamic acid, methyl ester	92
7-[3-[(cyclobutylcarbonyl)amino]phenyl]-pyrazolo[1,5-a]pyrimidine-3-carboxylic acid, ethyl ester	82

The novel compounds of this invention have also been shown to have skeletal muscle relaxant activity through the use of two tests. The first test measures the effect of representative compounds on the ability of rats to remain on an inclined screen. Groups of at least 6 rats were treated orally with graded doses of test compounds or vehicle and placed on a wire mesh screen (inclined at an angle of 60° from a horizontal level) 65 minutes later. The number of rats falling off the screen within 30 minutes was recorded. The ED_{50} (dose necessary to cause 50% of the animals tested to fall off) was calculated according to the linear arcsine transformation method of Finney, D. J., "Statistical Methods in Biological Assay", 2nd Ed., Hafner, N.Y., 1964, p. 454. Compounds were dissolved or suspended in a 2% aqueous starch suspension containing 5% polyethylene glycol 400 and a drop of polysorbate 80, and administered in a constant volume of 5 ml/kg. The results of representative compounds of this invention appear in Table IV.

TABLE IV

Effect on Ability of Rats to Remain on an Inclined Screen	
Compound	ED_{50} (mg/kg)
N—[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N—ethylpropanamide	4.6
N—[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N—ethylacetamide	3.9

The second test to illustrate that the novel compounds of the present invention possess skeletal muscle relaxant properties shows the effect of representative compounds on the locomotor activity in rats. Groups of 6 rats were treated orally with vehicle (5 ml/kg) or graded doses of the test compounds. Sixty minutes later, individual rats were placed in Actophotometers and locomotor activity was measured for 5 minutes after a brief (30 sec.) habituation period. Motor activity counts (number of crossings of the photo cells) were recorded for each rat, and mean activity counts were calculated for each treatment group. The dose causing a 50% decrease in mean activity counts compared with the vehicle group (MDD_{50}) was calculated from a linear regression equation. The test results of representative compounds appear in Table V.

TABLE V

Effects on Locomotor Activity in Rats	
Compound	MDD_{50} (mg/kg P.O.)
N—[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N—ethylpropanamide	2.0
N—[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N—ethylacetamide	1.4

The novel compounds of the present invention have been found to be highly useful for drug therapy in mammals when administered in amounts ranging from about 0.1 mg to about 20.0 mg/kg of body weight per day. A preferred dosage regimen for optimum results would be from about 0.5 mg to about 10.0 mg/kg of body weight per day. Dosage units are employed such that a total of from about 10 to about 700 mg of active compound for a subject of about 70 kg of body weight are administered in a 24 hour period. This dosage regimen may be adjusted to provide the optimum therapeutic response. For example, several divided doses may be administered daily or the dose may be proportionally reduced as indicated by the exigencies of the therapeutic situation. The compounds of this invention are preferably administered orally but may be administered in any convenient manner such as by the intravenous, intramuscular, or subcutaneous routes.

Compositions according to the present invention having the desired clarity, stability and adaptability for parenteral use are obtained by dissolving from 0.10% to 10.0% by weight of active compound in a vehicle consisting of a polyhydric aliphatic alcohol or mixtures thereof. Especially satisfactory are glycerin, propylene glycol, and polyethylene glycols. The polyethylene glycols consist of a mixture of nonvolatile, normally liquid, polyethylene glycols which are soluble in both water and organic liquids and which have molecular weights of from about 200 to 1500. Although the amount of active compound dissolved in the above vehicle may vary from 0.10% to 10.0% by weight, it is preferred that the amount of active compound employed be from about 3.0% to about 9.0% by weight. Although various mixtures of the aforementioned nonvolatile polyethylene glycols may be employed, it is preferred to use a mixture having an average molecular weight of from about 200 to about 400.

In addition to the active compound, the parenteral solutions may also contain various preservatives which may be used to prevent bacterial and fungal contamination. The preservatives which may be used for these purposes are, for example, myristyl-gamma-picolinium chloride, benzalkonium chloride, phenethyl alcohol, p-chlorophenyl-alpha-glycerol ether, methyl and propyl parabens, and thimerosal. As a practical matter, it is also convenient to employ antioxidants. Suitable antioxidants include, for example, sodium bisulfite, sodium metabisulfite, and sodium formaldehyde sulfoxylate. Generally, from about 0.05% to about 0.2% concentrations of antioxidant are employed.

For intramuscular injection, the preferred concentration of active compound is 0.25 to 0.50 mg/ml of the final compositions. The novel compounds of the present invention are equally adapted to intravenous administration when diluted with water or diluents employed in intravenous therapy such as isotonic glucose in appro-

priate quantities. For intravenous use, initial concentrations down to about 0.05 to 0.25 mg/ml of active ingredient are satisfactory.

The active compounds of the present invention may be orally administered, for example, with an inert diluent or with an assimilable edible carrier, or they may be enclosed in hard or soft shell gelatin capsules, or compressed into tablets, or incorporated directly into the food of the diet. For oral therapeutic administration, the active compounds may be incorporated with excipients and used in the form of tablets, troches, capsules, elixirs, suspensions, syrups, wafers and the like. Additionally, the active ingredient may be incorporated with the proper pharmaceutical carrier or carriers known in the art to produce a sustained-release tablet or capsule. Such compositions and preparations should contain at least 0.1% of active compound. The percentage of the compositions and preparations may, of course, be varied and may conveniently be between about 2% to about 60% of the weight of the unit dose. The amount of active compound in such therapeutically useful compositions is such that a suitable dosage will be obtained.

The tablets, troches, pills, capsules and the like may also contain one or more of the following: a binder such as gum tragacanth, acacia, corn starch or gelatin; excipients such as dicalcium phosphate; a disintegrating agent such as corn starch, potato starch, alginic acid and the like; a lubricant such as magnesium stearate; a wetting agent such as sodium lauryl sulfate and a sweetening agent such as sucrose, lactose or saccharin may be added or a flavoring agent such as peppermint, oil of wintergreen or cherry flavoring. When the dosage unit form is a capsule, it may contain, in addition to materials of the above type, a liquid carrier such as a fatty oil. Various other materials may be present as coatings or to otherwise modify the physical form of the dosage unit. For instance, tablets, pills or capsules may be coated with shellac, sugar or both. A syrup or elixir may contain the active compound, sucrose as a sweetening agent, methyl and propylparabens as preservatives, a dye and flavoring such as cherry or orange flavor. Of course, any material used in preparing any dosage unit form should be pharmaceutically pure and substantially nontoxic in the amounts employed.

The following non-limiting examples illustrate the preparation of representative compounds of the present invention.

EXAMPLE 1

N-[3-[3-(Dimethylamino)-1-oxo-2-propenyl]phenyl]-propanamide

A 20 g portion of N-(3-acetylphenyl)propanamide in 50 ml of dimethylformamide dimethylacetal was refluxed for 8 hours, then evaporated. The residue was taken up in 200 ml of dichloromethane, passed through hydrous magnesium silicate, diluted with hexane and concentrated, giving 21.17 g of the desired compound.

Following the procedure of Example 1 and using the indicated starting materials, the amides of Examples 2–5, found in Table VI, were prepared.

TABLE VI

Ex.	Starting Material	Amide
2	N—(3-acetylphenyl)-ethanamide	N—[3-(3-dimethylamino)-1-oxo-2-propenyl)phenyl]-acetamide
3	(3-acetylphenyl)carbamic acid, methyl ester	[3-[3-dimethylamino)-1-oxo-2-propenyl]phenyl]-carbamic acid, methyl ester
4	(3-acetylphenyl)carbamic acid, butyl ester	[3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]-carbamic acid, butyl ester
5	N—(3-acetylphenyl)-butanamide	N—[3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]-butanamide

EXAMPLE 6

N-[3-[3-(Dimethylamino)-1-oxo-2-propenyl]phenyl-N-ethylpropanamide

A mixture of 3.47 g of N-[3-[3-(dimethylamino)-oxo-2-propenyl]phenyl]propanamide and 0.68 g of 60% sodium hydride in oil in dimethylformamide was stirred for 0.5 hour under argon, then cooled in an ice bath and a solution of 2.4 g of ethyl iodide in 10 ml of dimethylformamide was added in small portions. The mixture was then stirred at room temperature for 0.5 hour and extracted three times with hexane. The extracts were discarded, water was added and this mixture extracted with dichloromethane. This extract was evaporated and the residue crystallized from hexane giving the desired compound, mp 105°–107° C.

Following the procedure of Example 6 using the compounds of Examples 1–5 and appropriate alkyl halides, the alkylated amides of Examples 7–12, found in Table VII, were prepared.

TABLE VII

Ex.	Starting Material of Ex.	Alkylated Amide	MP °C.
7	2	N—[3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]-N—ethylacetamide	110–113
8	1	N—[3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]-N—methylpropanamide	148–149
9	2	N—[3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]-N—propylacetamide	110–112
10	3	[3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]methylcarbamic acid, methyl ester	93–95
11	3	[3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]ethylcarbamic acid, methyl ester	95–97
12	2	N—[3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]-N—methylacetamide	146–148

EXAMPLE 13

N-[3-(3-Cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N-ethylpropanamide

A mixture of 0.54 g of 3-amino-4-pyrazolecarbonitrile and 1.37 g of N-[3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]-N-ethylpropanamide in 50 ml of glacial acetic acid was refluxed for 8 hours and then the solvent was removed. The residue was partitioned between saturated aqueous sodium bicarbonate and dichloromethane. The organic layer was separated, dried, passed through a pad of hydrous magnesium silicate and hexane was added to the refluxing filtrate. The mixture was then cooled and the solid collected, giving 1.3 g of the desired product, mp 161°–162° C.

Following the procedure of Example 13 and using appropriately substituted 3-amino-pyrazoles together

with the indicated intermediates, the products of Examples 14–37 found in Table VIII were prepared.

TABLE VIII

Ex.	Intermediate of Ex.	3-Amino-pyrazole	Product	MP °C.
14	7	3-aminopyrazole-4-carbonitrile	N—[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N—ethylacetamide	186–187
15	7	3-aminopyrazole	N—ethyl-N—(3-pyrazolo[1,5-a]pyrimidin-7-ylphenyl)acetamide	115–117
16	9	3-aminopyrazole	N—propyl-N—(3-pyrazolo[1,5-a]pyrimidin-7-ylphenyl)acetamide	90–92
17	9	3-aminopyrazole-4-carbonitrile	N—[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N—propylacetamide	151–153
18	6	ethyl-3-amino-pyrazole-4-carboxylate	7-[3-[ethyl(1-oxopropyl)amino]phenyl]pyrazolo[1,5-a]pyrimidine-3-carboxylic acid, ethyl ester	124–126
19	10	3-aminopyrazole-4-carbonitrile	[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]methylcarbamic acid, methyl ester	168–170
20	10	ethyl-3-amino-pyrazole-4-carboxylate	7-[3-[(methoxycarbonyl)methyl-amino]phenyl]pyrazolo[1,5-a]pyrimidine-3-carboxylic acid, ethyl ester	115–116
21	3	3-aminopyrazole-4-carbonitrile	[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]carbamic acid, methyl ester	256–258
22	4	3-aminopyrazole-4-carbonitrile	[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]carbamic acid, butyl ester	131–133
23	1	3-aminopyrazole	N—[3-(pyrazolo[1,5-a]pyrimidin-7-yl)phenyl]propanamide	177–178
24	1	3-aminopyrazole-4-carbonitrile	N—[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]propanamide	202–204
25	1	3-amino-5-methylpyrazole-4-carbonitrile	N—[3-(3-cyano-2-methylpyrazolo[1,5-a]-pyrimidin-7-yl)phenyl]propanamide	177–178
26	8	3-aminopyrazole-4-carbonitrile	N—[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N—methylpropanamide	
27	8	3-amino-5-methylpyrazole-4-carbonitrile	N—[3-(3-cyano-2-methylpyrazolo[1,5-a]-pyrimidin-7-yl)phenyl]-N—methyl-propanamide	184–186
28	5	3-aminopyrazole-4-carbonitrile	N—[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]butanamide	138–140
29	12	3-aminopyrazole-4-carbonitrile	N—[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N—methylacetamide	195–197
30	2	3-aminopyrazole-4-carbonitrile	N—[3-(3-cyanopyrazolo[1,5-a]pyrimidine-7-yl)phenyl]acetamide	257–259
31	12	3-aminopyrazole	N—methyl-N—(3-pyrazolo[1,5-a]pyrimidine-7-ylphenyl)acetamide	118–120
32	12	ethyl-3-amino-pyrazole-4-carboxylate	7-[3-(acetylmethylamino)phenyl]pyrazolo-[1,5-a]pyrimidine-3-carboxylic acid, ethyl ester	155–156
33	7	3-amino-4-carbo-ethoxypyrazole	7-[3-(acetylethylamino)phenyl]pyrazolo-[1,5-a]pyrimidine-3-carboxylic acid, ethyl ester	147–148
34	2	3-amino-4-carbo-ethoxypyrazole	7-[3-(acetylamino)phenyl]pyrazolo[1,5-a]-pyrimidine-3-carboxylic acid, ethyl ester	202–204
35	3	3-amino-4-carbo-ethoxypyrazole	7-[3-[(methoxycarbonyl)amino]phenyl]-pyrazolo[1,5-a]pyrimidine-3-carboxylic acid, ethyl ester	187–188
36	10	3-aminopyrazole	methyl(3-pyrazolo[1,5-a]pyrimidin-7-ylphenyl)carbamic acid, methyl ester	107–109
37	9	3-amino-4-carbo-ethoxypyrazole	7-[3-(acetylpropylamino)phenyl]pyrazolo-[1,5-a]pyrimidine-3-carboxylic acid, ethyl ester	156–157

EXAMPLE 38

N-[3-(3-Chloropyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N-ethylacetamide

A mixture of 1.0 g of N-ethyl-N-(3-pyrazolo[1,5-a]pyrimidin-7-ylphenyl)acetamide and 4.57 g of 1-chlorobenzotriazole in 50 ml of dichloromethane was refluxed for 25 minutes, then cooled and poured into 50 ml of ice-cold 2.5N aqueous sodium hydroxide. The mixture was filtered through hydrous magnesium silicate, precipitated with hexane and the solid collected, giving 0.7 g of the desired product, mp 157°–159°C.

EXAMPLE 39

7-[3-[Ethyl(methoxycarbonyl)amino]phenyl]-pyrazolo[1,5-a]pyrimidine-3-carboxylic acid, ethyl ester

A 12.41 g portion of [3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]carbamic acid, methyl ester was reacted as described in Example 6, using 9.36 g of ethyliodide, giving 13.4 g of [3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]ethylcarbamic acid, methyl ester, mp 95°–97° C.

A 2.76 g portion of the above ester was reacted with 1.55 g of ethyl-3-aminopyrazole-4-carboxylate as described in Example 13, giving 2.87 g of the desired product, mp 117°–119 C.

EXAMPLE 40

[3-(3-Cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]ethylcarbamic acid, methyl ester

A 2.76 g portion of [3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]ethylcarbamic acid, methyl ester was reacted with 1.08 g of 3-aminopyrazole-4-carbonitrile as described in Example 13, giving 2.6 g of the desired product, mp 162°–164° C.

EXAMPLE 41

[3-(3-Cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]methylcarbamic acid, ethyl ester

1-Acetylphenyl-3-carbamic acid, ethyl ester was converted to [3-[3-(dimethylamino)-1-oxo-2-propenyl]-phenyl]carbamic acid, ethyl ester by the procedure of Example 1 and this ester was then reacted with methyl iodide, again by the procedure of Example 6, giving [3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]methylcarbamic acid, ethyl ester.

A 2.6 g portion of the above ester was reacted with 1.08 g of 3-aminopyrazole-4-carbonitrile by the procedure of Example 13, giving 2.09 g of the desired compound, mp 140°–142° C.

EXAMPLE 42

Ethyl(3-pyrazolo[1,5-a]pyrimidin-7-ylphenyl)carbamic acid, ethyl ester

[3-[3-(Dimethylamino)-1-oxo-2-propenyl]phenyl]carbamic acid was reated with ethyl iodide by the procedure of Example 6, giving [3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]ethylcarbamic acid, ethyl ester.

A 2.9 g portion of the above ester was reacted with 0.83 g of 3-aminopyrazole by the procedure of Example 13, giving 2.27 g of the desired product, mp 79°–81° C.

EXAMPLE 43

[3-(3-Cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]ethylcarbamic acid, ethyl ester

A 2.0 g portion of [3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]ethylcarbamic acid, ethyl ester was reacted with 1.08 g of 3-aminopyrazole-4-carbonitrile as described in Example 13, giving 2.52 g of the desired product, mp 133°–135° C.

EXAMPLE 44

[3-(3-Chloropyrazolo[1,5-a]pyrimidin-7-yl)phenyl]ethylcarbamic acid, ethyl ester

A 1.55 g portion of ethyl(3-pyrazolo[1,5-a]-pyrimidin-7-ylphenyl)carbamic acid, ethyl ester in 50 ml of dichloromethane was reacted with 1-chlorobenzotriazole for 30 minutes, giving 1.29 g of the desired product, mp 100°–102° C.

EXAMPLE 45

N-[3-(3-Cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N-2-propenylacetamide

An 11.61 g portion of N-[3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]acetamide was reacted with 7.26 g of allyl bromide as described in Example 6, giving 13.34 g of N-[3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]-N-2-propenylacetamide, mp 91°–94° C.

A 1.36 g portion of the above intermediate was reacted with 0.54 g of 3-aminopyrazole-4-carbonitrile as described in Example 13, giving 1.0 g of the desired compound, mp 135°–137° C.

EXAMPLE 46

N-[3-(3-Cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N-2-propynylacetamide

An 11.61 g portion of N-[3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]acetamide was reacted with propynyl bromide as described in Example 6, giving N-[3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]-N-2-propynylacetamide, mp 98°–101° C.

A 2.7 g portion of the above intermediate was reacted with 1.08 g of 3-aminopyrazole-4-carbonitrile as described in Example 13, giving 1.90 g of the desired product, mp 193°–195° C.

EXAMPLE 47

N-Butyl-N-[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]acetamide

An 11.61 g portion of [3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]carbamic acid, methyl ester was reacted with 11.0 g of butyl iodide by the procedure of Example 6, giving 16.3 g. of N-butyl-N-[3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]acetamide.

A 2.88 g portion of the above intermediate was reacted with 1.08 g of 3-aminopyrazole-4-carbonitrile by the procedure of Example 13, giving 1.61 g of the desired product, mp 146°–148° C.

EXAMPLE 48

N-[3-(3-Cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N-methylcarbamic acid, butyl ester

An 11.61 g portion of [3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]carbamic acid, butyl ester was reacted with 6.82 g of methyl iodide by the procedure of Example 6, giving 11.67 g of [3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]methylcarbamic acid, butyl ester.

A 3.04 g portion of the above ester was reacted with 1.08 g of 3-aminopyrazole-4-carbontirile as described in Example 13, giving 2.3 g of the desired product, mp 96°–97° C.

EXAMPLE 49

N-[3-(3-Chloropyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N-methylacetamide

A 1.0 g portion of N-methyl-N-(3-pyrazolo[1,5-a]pyrimidin-7-ylphenyl)acetamide was reacted as described in Example 38, giving 1.0 g of the desired product, mp 163°–165° C.

EXAMPLE 50

[3-(3-Chloropyrazolo1,5-a]pyrimidin-7-yl)phenyl]methylcarbamic acid, methyl ester

A 1.4 g portion of methyl(3-pyrazolo[1,5-a]pyrimidin-7-ylphenyl)carbamic acid, methyl ester was reacted as described in Example 38, giving 1.42 g of the desired product, mp 132°–134° C.

EXAMPLE 51

7-[3-[(Cyclopropylcarbonyl)methylamino]phenyl-pyrazolo[1,5-a]pyrimidine-3-carboxylic acid, ethyl ester

N-(3-Acetylphenyl)cyclopropanecarboxamide was prepared by the reaction of m-aminoacetophenone, diisopropylethylamine and cyclopropanecarboxylic acid chloride in dichloromethane.

This compound was then converted to N-[3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]cyclopropanecarboxamide by the procedure of Example 1 and then alkylated by the procedure of Example 6, using methyl iodide, giving 10.17 g of N-[3-(3-dimethylamino)-1-oxo-2-propenyl)phenyl]-N-methylcyclopropanecarboxamide, mp 120°–122° C.

A 0.54 g portion of this compound was reacted as described in Example 13 with 3-aminopyrazole-4-carbonitrile, giving 1.08 g of the desired product, mp 178°–180° C.

EXAMPLE 52

7-[3-[(Cyclopropylcarbonyl)methylamino]phenyl-pyrazolo[1,5-a]pyrimidine-3-carboxylic acid, ethyl ester

A 0.73 g portion of ethyl 3-aminopyrazole-4-carboxylate and 1.36 g of N-[3-[(3-(dimethylamino)-1-oxo-2-propenyl]phenyl]-N-methylcyclopropanecarboxamide were reacted as described in Example 13, giving 0.52 g of the desired product, mp 122°–124° C.

EXAMPLE 53

N-[3-(3-Cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N-methylcyclobutanecarboxamide

m-Aminoacetophenone, cyclobutanecarboxylic acid, chloride and diisopropylethylamine in dichloromethane were reacted, giving N-(3-acetylphenyl)cyclobutanecarboxamide.

This compound was then converted to N-[3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]cyclobutanecarboxamide, mp 155°–157° C., by the procedure of Example 1 and further alkylated by the procedure of Example 6, using methyl iodide to give 8.32 g of N-[3-[3-(dimethylamino)1-oxo-2-propenyl]phenyl]-N-methylcyclobutanecarboxamide, mp 117°–119° C.

A 0.54 g portion of 3-aminopyrazole-4-carbonitrile was reacted with 1.43 g of the above product by the procedure of Example 13, giving 1.3 g of the desired product, mp 157°–158° C.

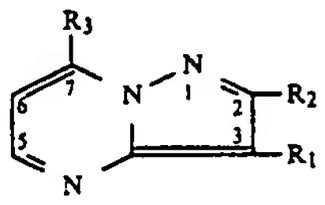
EXAMPLE 54

7-[3-[(Cyclobutylcarbonyl)amino]phenyl]pyrazolo[1,5-a]pyrimidine-3-carboxylic acid, ethyl ester

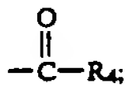
A 0.78 g portion of 3-amino-4-carboethoxypyrazole ard 1.36 g of N-[3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]cyclobutanecarboxamide were reacted as described in Example 13, giving 1.52 g of the desired product, mp 123°–125° C.

What is claimed is:

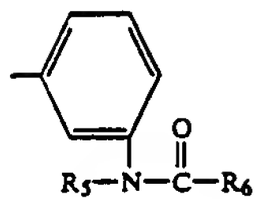
1. A compound of the formula:



wherein $R_1$is selected from the group consisting of hydrogen, halogen, cyano and

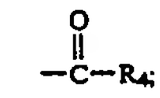


R_2 is selected from the group consisting of hydrogen and alkyl (C_1–C_3); R_3 is



R_4 is selected from the group consisting of hydrogen, alkyl(C_1–C_6) and alkoxy(C_1–C_6); R_5 is selected from the group consisting of hydrogen, alkyl(C_1–C_6), alkenyl(C_2–C_6), —$CH_2C{\equiv}CH$, cycloalkyl(C_3–C_6)methyl, —CH_2OCH_3 and —$CH_2CH_2OCH_3$; and R_6 is selected from the group consisting of alkyl(C_1–C_6), cycloalkyl(C_3–C_6), —O-alkyl(C_1–C_6), —NH-alkyl(C_1–C_3), —N-dialkyl(C_1–C_3), —$(CH_2)_n$—O-alkyl(C_1–C_3), —$(CH_2)_n$—NH-alkyl(C_1–C_3) and —$(CH_2)_n$—N-dialkyl(C_1–C_3), where n is an integer 1 to 3 inclusive.

2. A compound according to claim 1, wherein R_1 is cyano or



R_2 is hydrogen; R_4 is alkyl(C_1–C_6), alkenyl(C_2–C_6) or —$CH_2{\equiv}CH$; and R_6 is alkyl (C_1–C_6), cycloalkyl(C_3–C_6) or —O-alkyl(C_1–C_6).

3. The compound according to claim 2, which is N-[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N-ethylpropanamide.

4. The compound according to claim 2, which is N-[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N-ethylacetamide.

5. The compound according to claim 2, which is N-[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N-propylacetamide.

6. The compound according to claim 2, which is [3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]methylcarbamic acid, methyl ester.

7. The compound according to claim 2, which is 7-[3-[(methoxycarbonyl)methylamino]phenyl]-pyrazolo[1,5-a]pyrimidine-3-carboxylic acid, ethyl ester.

8. The compound according to claim 2, which is [3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]ethylcarbamic acid, methyl ester.

9. The compound according to claim 2, which is ethyl(3-pyrazolo[1,5-a]pyrimidin-7-ylphenyl)carbamic acid, ethyl ester.

10. The compound according to claim 2, which is [3-(3-chloropyrazolo[1,5-a]pyrimidin-7-yl)phenyl]ethylcarbamic acid, ethyl ester.

11. The compound according to claim 2, which is N-[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N-2-propenylacetamide.

12. The compound according to claim 2, which is N-[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N-2-propynylacetamide.

13. The compound according to claim 2, which is N-[3-(3-cyanopyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N-methylacetamide.

14. A method of ameliorating anxiety in a mammal which comprises administering to said mammal an amount of a compound of claim 1 sufficient to reduce anxiety.

15. A composition of matter in dosage unit form comprising from 2–750 mg of a compound of claim 1 in association with a pharmaceutically acceptable carrier.

* * * * *

EXHIBIT C

United States Patent [19]

Dusza et al.

[11] **Patent Number: 4,521,422**

[45] **Date of Patent: Jun. 4, 1985**

[54] **ARYL AND HETEROARYL[7-(ARYL AND HETEROARYL)PYRAZOLO[1,5-a]PYRIMIDIN-3-YL]METHANONES**

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[73] Assignee: **American Cyanamid Company**, Stamford, Conn.

[21] Appl. No.: **612,812**

[22] Filed: **May 24, 1984**

Related U.S. Application Data

[63] Continuation-in-part of Ser. No. 506,966, Jun. 23, 1983, abandoned.

[51] **Int. Cl.**[3] **C07D 487/04; A61K 31/505**

[52] **U.S. Cl.** **514/258**; 544/281; 514/906

[58] **Field of Search** 544/281; 424/251

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Attorney, Agent, or Firm—Anne M. Rosenblum

[57] **ABSTRACT**

Aryl and heteroaryl[7-(aryl and heteroaryl)-pyrazolo[1,5-a]pyrimidin-3-yl]methanones which are new compounds active as anxiolytic, anticonvulsant, sedative-hypnotic and skeletal muscle relaxant agents in mammals and the novel process of making these compounds.

31 Claims, No Drawings

ARYL AND HETEROARYL[7-(ARYL AND HETEROARYL)PYRAZOLO[1,5-a]PYRIMIDIN-3-YL]METHANONES

CROSS REFERENCE TO RELATED APPLICATION

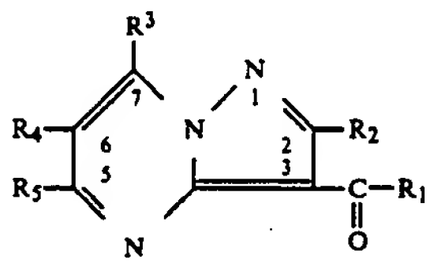
This application is a continuation-in-part of our co-pending application, Ser. No. 506,966, filed June 23, 1983, now abandoned.

SUMMARY OF THE INVENTION

This invention relates to new organic compounds which are aryl or heteroaryl[7-(aryl or heteroaryl)-pyrazolo[1,5-a]pyrimidin-3-yl]methanones which are useful as anxiolytic or antiepileptic agents as well as sedative-hypnotic and skeletal muscle relaxant agents. This invention also relates to these methods of using the novel compounds, to compositions of matter containing them as the active ingredient and to processes for their production.

DETAILED DESCRIPTION OF THE INVENTION

In accordance with this invention, the novel compounds are represented by the following structural formula:



wherein R_1 is selected from the group consisting of unsubstituted phenyl; phenyl mono- or di-substituted by halogen, alkoxy(C_1–C_3) or alkyl(C_1–C_3); phenyl mono-substituted by trifluoromethyl, alkylthio(C_1–C_3), alkylamino(C_1–C_3), dialkylamino(C_1–C_3), methylenedioxy, alkylsulfonyl(C_1–C_3) or alkanoylamino(C_1–C_3); naphthalenyl; thiazolyl; biphenyl; thienyl; furanyl; pyridinyl; substituted thiazolyl; substituted biphenyl; substituted thienyl; and substituted pyridinyl wherein the substituents are selected from one or two of the group consisting of halogen, alkoxy(C_1–C_3) and alkyl(C_1–C_3); R_2, R_4 and R_5 are each selected from the group consisting of hydrogen and alkyl(C_1–C_3); and R_3 is selected from the group consisting of unsubstituted phenyl, phenyl mono-substituted by halogen, trifluoromethyl, alkoxy(C_1–C_3), amino, alkyl(C_1–C_3), alkylamino(C_1–C_6), dialkylamino(C_1–C_3), alkanoylamino(C_1–C_6), N-alkyl(C_1–C_6)alkanoylamino(C_1–C_6), cyano or alkylthio(C_1–C_3); furanyl; thienyl; pyridinyl; and pyridine-1-oxide.

The most preferred compounds of this invention of particular interest are those compounds of the above formula wherein R_3 is 3-(trifluoromethyl)phenyl, 3-pyridinyl or 4-pyridinyl especially when R_1 is 2-furanyl and R_2, R_4 and R_5 are each hydrogen. Also, the compounds of major interest are selected from the above formula wherein R_3 is 3-(trifluoromethyl)phenyl, 3-pyridinyl, 4-pyridinyl, 3-[N-alkyl(C_1–C_6)alkanoylamino(C_1–C_6)]phenyl or 3-[alkylamino(C_1–C_6)], when R_1 is unsubstituted phenyl; phenyl substituted by 4-methyl, 4-ethyl, 4-methoxy, 3,4-dimethoxy or 4-dimethylamino; 2-furanyl; 2-thienyl; 2-pyridinyl; or 4-pyridinyl; and R_2, R_4 and R_5 are each hydrogen.

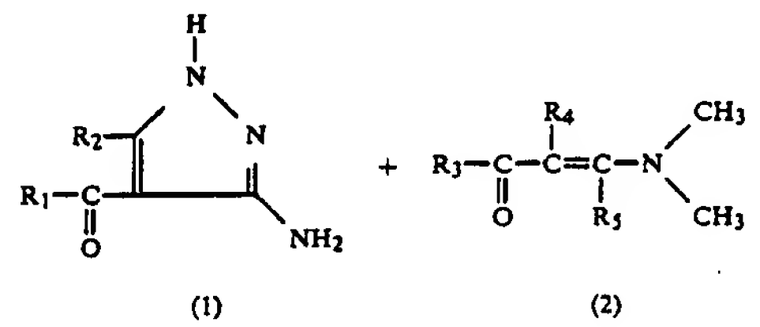
Other representative compounds of the invention herein are as follows:

2-furanyl[7-(2-furanyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
2-furanyl[7-(2-thienyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
[7-(2-furanyl)pyrazolo[1,5-a]pyrimidin-3-yl]-2-pyridinyl-methanone
[7-(2-furanyl)pyrazolo[1,5-a]pyrimidin-3-yl]-3-pyridinyl-methanone
[7-(2-furanyl)pyrazolo[1,5-a]pyrimidin-3-yl]-4-pyridinyl-methanone
[4-(dimethylamino)phenyl][7-(2-furanyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
2-thienyl[7-(2-thienyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
3-pyridinyl[7-(2-thienyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
[4-(dimethylamino)phenyl][7-(2-thienyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
2-furanyl[7-(3-thienyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
2-thienyl[7-(3-thienyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
3-pyridinyl[7-(3-thienyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
4-pyridinyl[7-(3-thienyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
[4-(dimethylamino)phenyl][7-(3-thienyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(3,4-dimethylphenyl)[7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(3,4-dimethylphenyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(3,4-dimethylphenyl)[7-[3-(trifluoromethyl)phenyl]-pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(4-dimethylaminophenyl)[7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(4-dimethylaminophenyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(4-dimethylaminophenyl)[7-[3-(trifluoromethyl)-phenyl]pyrazolo[1,5-a]pyrimidin-3-yl]methanone
2-thiazolyl[7-[3-trifluoromethyl)phenyl]pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(5-methyl-2-thienyl)[7-[3-(trifluoromethyl)phenyl]-pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(5-methyl-2-thienyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(5-methyl-2-thienyl)[7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(5-chloro-2-thienyl)[7-[3-(trifluoromethyl)phenyl]-pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(5-chloro-2-thienyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(5-chloro-2-thienyl)[7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(5-bromo-2-thienyl)[7-[3-(trifluoromethyl)phenyl]-pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(5-bromo-2-thienyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(5-bromo-2-thienyl)[7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(3-chloro-2-pyridinyl)[7-[3-(trifluoromethyl)phenyl]-pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(3-chloro-2-pyridinyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone

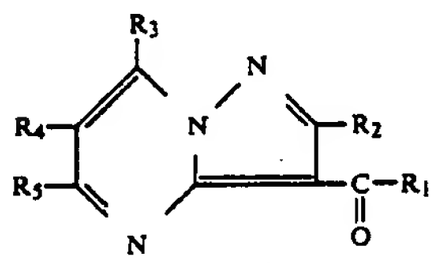
(3-chloro-2-pyridinyl)[7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(3-fluoro-2-pyridinyl)[7-[3-(trifluoromethyl)phenyl]-pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(3-fluoro-2-pyridinyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(3-fluoro-2-pyridinyl)[7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(5-chloro-2-pyridinyl)[7-[3-(trifluoromethyl)phenyl]-pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(5-chloro-2-pyridinyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(5-chloro-2-pyridinyl)[7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(5-fluoro-2-pyridinyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(5-fluoro-2-pyridinyl)[7-[3-(trifluoromethyl)phenyl]-pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(3-methyl-2-pyridinyl)[7-[3-(trifluoromethyl)phenyl]-pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(3-methyl-2-pyridinyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(3-methyl-2-pyridinyl)[7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(5-methyl-2-pyridinyl)[7-[3-(trifluoromethyl)phenyl]-pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(2-fluorophenyl)[7-[3-(trifluoromethyl)phenyl]-pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(2-fluorophenyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(2-fluorophenyl)[7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(3-pyridinyl)[7-[3-(trifluoromethyl)phenyl]-pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(3-pyridinyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(3-pyridinyl)[7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(5-methyl-3-pyridinyl)[7-[3-(trifluoromethyl)phenyl]-pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(5-methyl-3-pyridinyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(5-methyl-3-pyridinyl)[7-(4-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl]methanone
(6-methyl-3-pyridinyl)[7-[3-(trifluoromethyl)phenyl]-pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(6-methyl-3-pyridinyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(6-methyl-3-pyridinyl)[7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(3-thienyl)[7-[3-(trifluoromethyl)phenyl]pyrazolo[1,5-a]pyrimidin-3-yl]methanone
[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]-3-thienyl-methanone
(3-furanyl)[7-[3-(trifluoromethyl)phenyl]pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(3-furanyl)[7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(3-methoxy-2-pyridinyl)[7-[3-(trifluoromethyl)phenyl]-pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(3-methoxy-2-pyridinyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(4-methoxy-2-pyridinyl)[7-[3-(trifluoromethyl)phenyl]-pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(4-methoxy-2-pyridinyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(4-methoxy-2-pyridinyl)[7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(4-methyl-2-pyridinyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(4-fluoro-2-pyridinyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(5-methoxy-2-pyridinyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(5-fluoro-3-pyridinyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(5-ethoxy-3-pyridinyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(5-ethoxy-2-pyridinyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(5-methoxy-3-pyridinyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(6-methoxy-3-pyridinyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
(6-methoxy-3-pyridinyl)[7-[3-(trifluoromethyl)phenyl]-pyrazolo[1,5-a]pyrimidin-3-yl]methanone
4-pyridinyl[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone
4-pyridinyl[7-[3-(trifluoromethyl)phenyl]pyrazolo[1,5-a]pyrimidin-3-yl]methanone

The instant invention is additionally concerned with the methods of treating anxiety or epilepsy and inducing a sedative-hypnotic or skeletal muscle relaxation effect in mammals employing the above-described compounds, to compositions of matter containing these compounds and processes for their production.

The novel compounds of this invention may be readily prepared as set forth in the following reaction scheme:



(1) (2)



(3)

wherein R_1, R_2, R_3, R_4, and R_5 are as described above. The reaction of an appropriately substituted pyrazole (1) and an appropriately substituted 3-dimethylamino-1-(aryl) or (heteroaryl)-2-propen-1-one (2) in glacial acetic acid at reflux temperature for several hours, followed by solvent removal, partitioning of the residue between saturated aqueous sodium bicarbonate and methylene chloride, passage of the organic layer through hydrous magnesium silicate and the addition of hexane to the refluxing eluate produces the desired products (3).

Products where R_3 is a pyridine-1-oxide may be prepared by treating the compounds (3) where R_3 is pyri-

dine with m-chloroperbenzoic acid in methylene chloride with stirring for several hours, collecting the solid, slurrying it in saturated aqueous sodium bicarbonate and boiling in water.

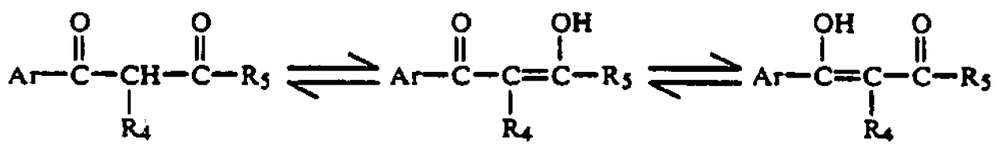
The substituted 3-dimethylamino-1-(aryl) or (heteroaryl)-2-propen-1-ones (2) are disclosed in one or more of U.S. Pat. Nos. 4,178,449; 4,281,000; and 4,236,005.

The substituted pyrazoles (1) are the subject of copending application, Ser. No. 507,317, filed June 23, 1983.

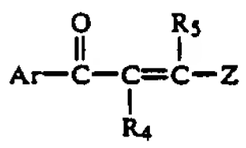
Pyrazolo[1,5-a]pyrimidines are prepared by condensation of 3-aminopyrazoles and substituted 3-aminopyrazoles with 1,3-dicarbonyl compounds as described in J. Med. Chem., 18, 645 (1974); J. Med. Chem., 18, 460 (1975); J. Med. Chem., 20, 386 (1977); Synthesis, 673 (1982) and references contained therein.

The 7-aryl and 7-heteroaryl[1,5-a]pyrimidines of this invention, which contain a 3-aroyl group, are synthesized by condensation of 1-aryl or 1-heteroaryl-1,3-dicarbonyl compounds with 3-amino-4-aroylpyrazoles.

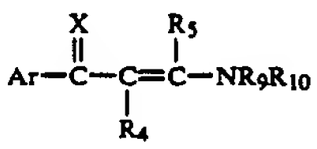
The 3-aryl-1,3-dicarbonyl compounds useful in condensations with the appropriate 3-amino-4-aroylpyrazoles are represented by the following structural formulae (4 to 8):



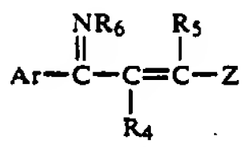
(4) (4a) (4b)



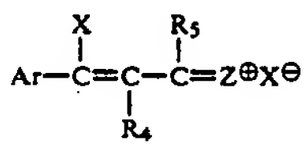
(5)



(6)



(7)



(8)

wherein R_4 and R_5 are hydrogen or alkyl(C_1–C_3); R_6 is alkyl(C_1–C_6), cyclohexyl, cyclopentyl, phenyl, or —$(CH_2)_m$-phenyl where m is an integer 1–3; X is chloro, bromo, OR_7 or SR_7, where R_7 is alkyl(C_1–C_6); Z is SR_7, OR_8, NR_9R_{10} or NHR_6 wherein R_8 is hydrogen, alkyl(C_1–C_{10}), —$(CH_2)_n$-phenyl where n is an integer 1–3, alkanoyl(C_2–C_{10}), benzoyl or carboalkoxy(C_2–C_{10}); and R_9 and R_{10} are individually selected from hydrogen, alkyl(C_1–C_{10}), phenyl and when taken together with the nitrogen atom to which they are attached form

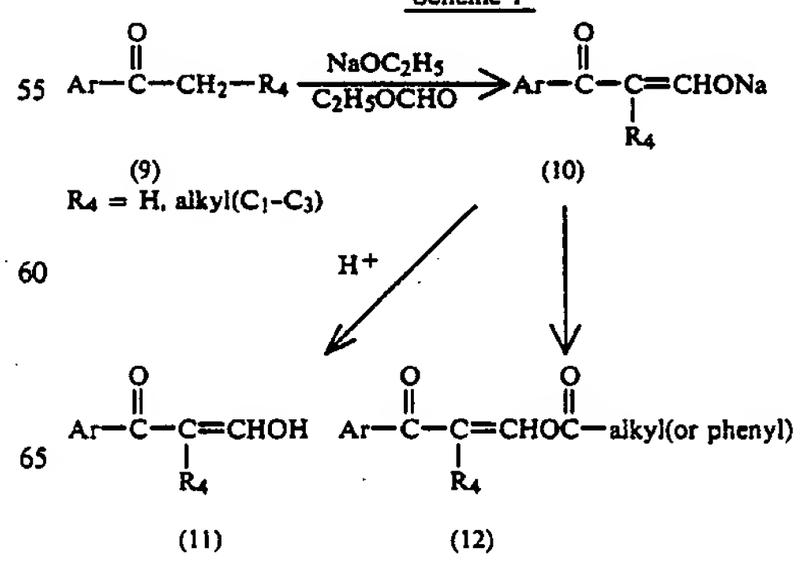
where p is an integer 4–6, or

where G is —O— or —N—D, where D is alkyl(C_1–C_6), benzyl, benzoyl or alkanoyl(C_2–C_7).

The structure represented by formula (4) is a 1-aryl-1,3-dicarbonyl derivative which may enolize to give two enol structures represented by formula (4a) and (4b). The extent of enolization is dependent on the substituent R_5. When R_5 is hydrogen, the structure (4) represents an α-formyl ketone derivative which exists principally as the enolized form (4a). Such hydroxymethyleneketones (4a) are prepared by formylation of arylketones (6) with alkali metal alkoxides and alkyl formates such as methyl formate, ethyl formate and the like. The preparation of hydroxymethyleneketones is illustrated in Scheme 1.

The intermediate alkali metal salts of hydroxymethyleneketones (10) can be acylated by reaction with acid chlorides or anhydrides such as alkanoyl chlorides, benzoyl chloride, alkanoic acid anhydrides or benzoic anhydride to give O-acyl derivatives (12). Neutralization of the alkali metal salts (10) with acids such as acetic acid, hydrochloric acid and the like affords hydroxymethyleneketones (11). Either the alkali metal salts (10), the hydroxymethyleneketones (11), or the O-acylated derivatives (12) or hydroxymethyleneketones may be condensed with 3-amino-4-aroylpyrazoles (1), under acidic or neutral conditions, in inert solvents, to give the novel 3-aroyl-7-aryl(or heteroaryl)-pyrazolo[1,5-a]pyrimidines (13) of this invention wherein R_4 is hydrogen or alkyl(C_1–C_3) and R_5 is hydrogen.

Scheme 1



(9) R_4 = H, alkyl(C_1–C_3)

(10)

(11)

(12) alkyl(or phenyl)

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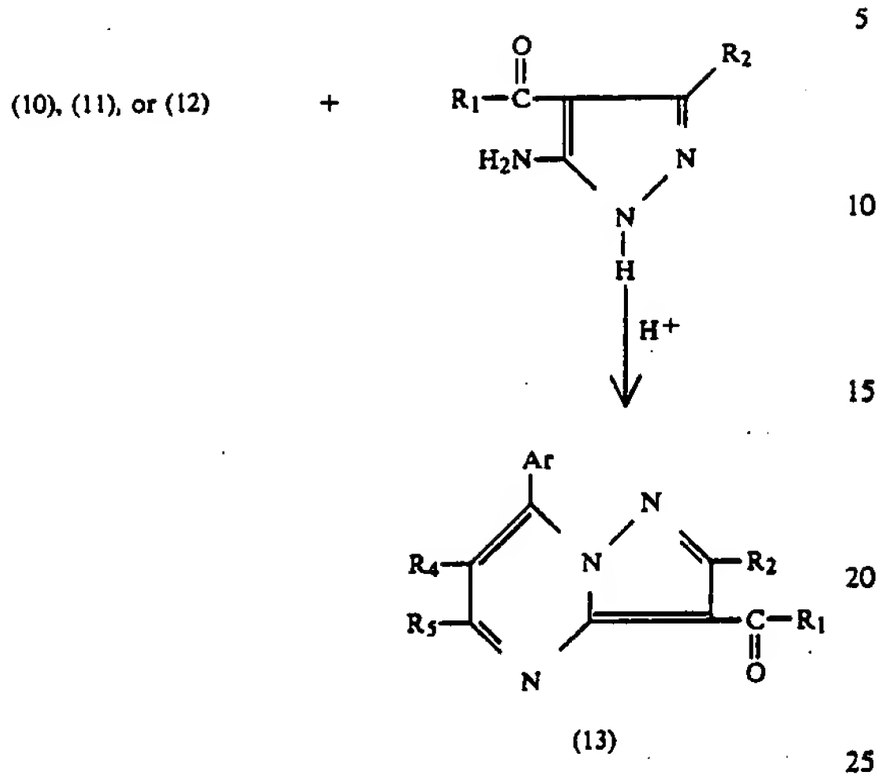
Scheme 1

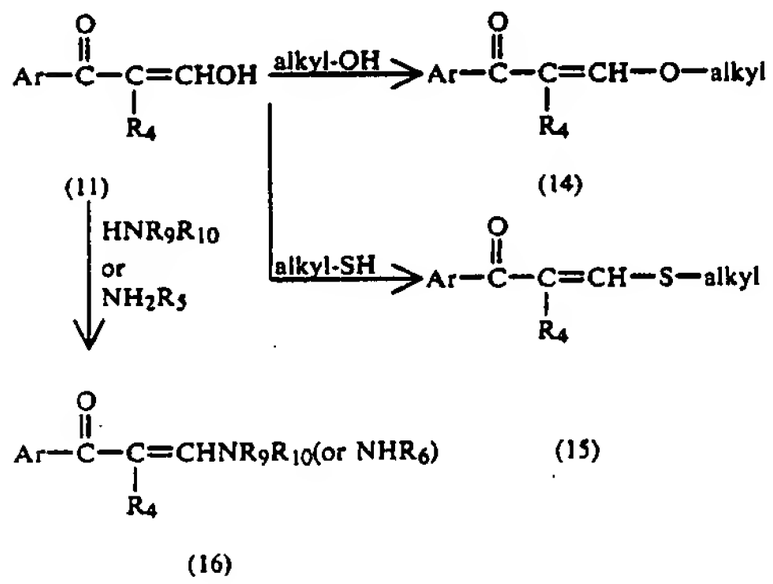


(13)

R_4 = hydrogen or alkyl(C_1–C_3)
R_5 = hydrogen

The hydroxymethyleneketones (11) may be converted by the procedure of Scheme 2 to other aldehyde equivalents such as alkoxymethyleneketones (14), alkylthiomethyleneketones (15), or aminomethyleneketones (16). These aldehyde equivalents of hydroxymethyleneketones on condensation with 3-amino-4-aroylpyrazoles give 3-aroyl-7-aryl(or heteroaryl)-pyrazolo[1,5-a]pyrimidines (13), wherein R_4 is hydrogen or alkyl(C_1–C_3) and R_5 is hydrogen.

Scheme 2



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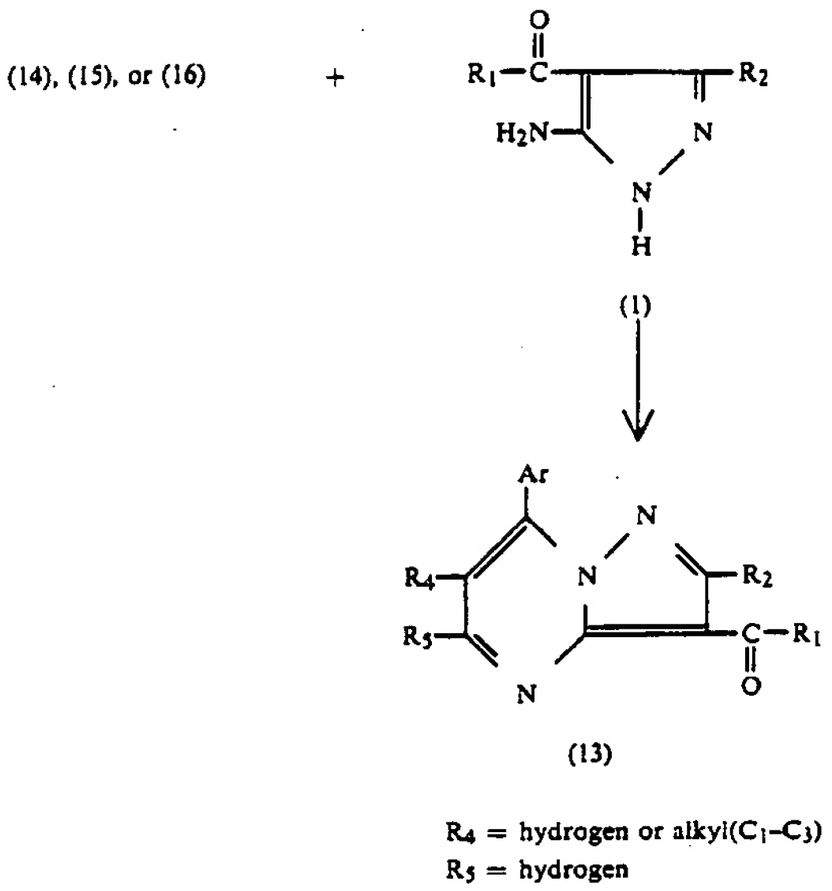
Scheme 2



(13)

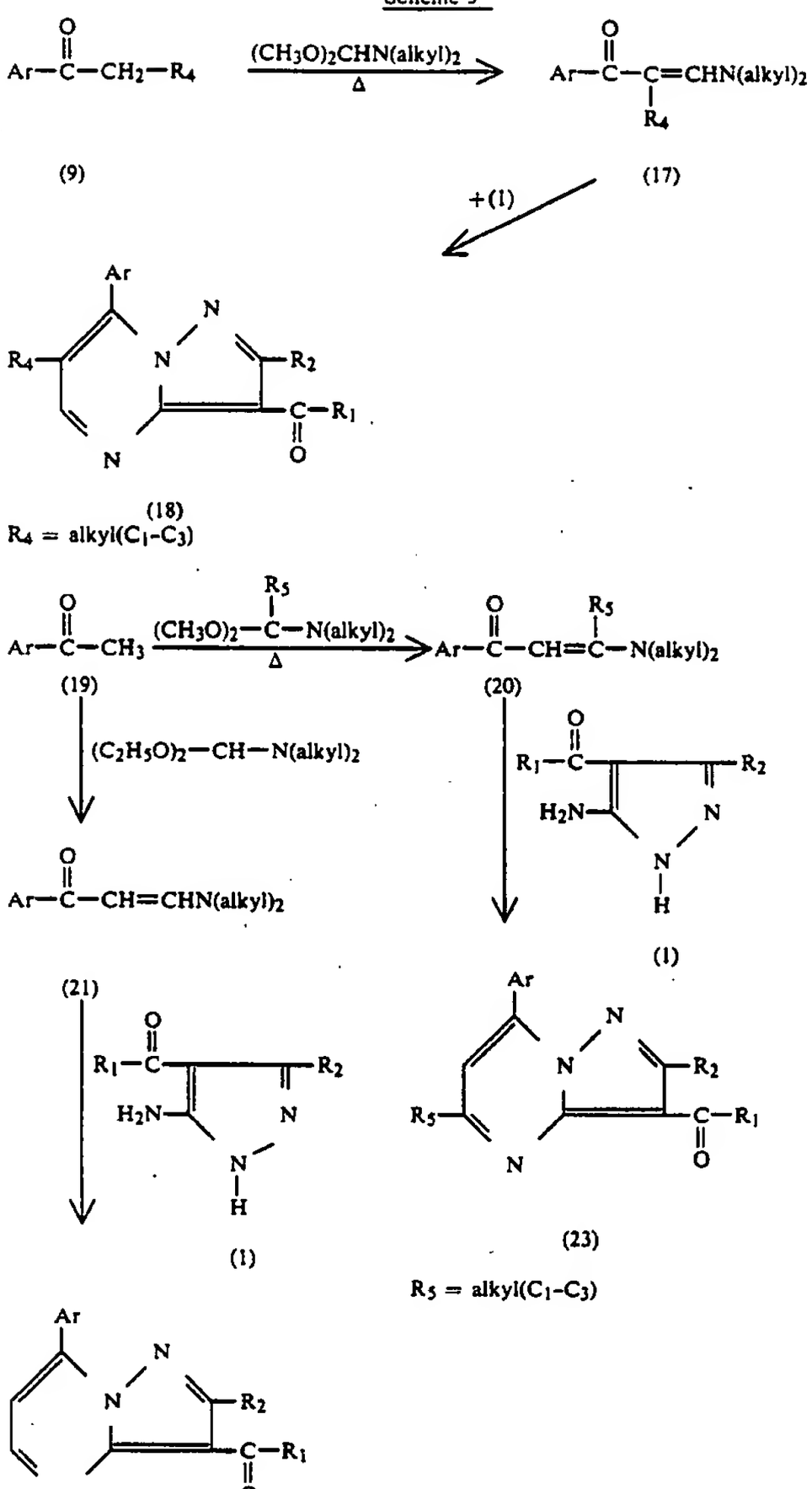
R_4 = hydrogen or alkyl(C_1–C_3)
R_5 = hydrogen

Thus, hydroxymethyleneketones and derivatives which are chemical equivalents of hydroxymethyleneketones react under acidic or neutral conditions with 3-amino-4-aroylpyrazoles to give novel 3-aroyl-7-aryl(or heteroaryl)pyrazolo[1,5-a]pyrimidines.

Other intermediates which are chemical equivalents of hydroxymethyleneketones (11) are 3-(dialkylamino)-1-aryl or (heteroaryl)-2-propen-1-ones (17). Such N,N-(dialkylamino)methyleneketones (enaminones) (17) are prepared by reaction of arylketones (9) with N,N-dimethylformamide-dialkoxyacetals or N,N-dimethylacetamide-dialkoxyacetals. Other acetals of N,N-dialkylformamides or acetals of N,N-dialkylacetamides, such as N,N-diethylformamide-dimethoxyacetal, N,N-dibutylformamide-diethoxyacetal, N,N-diethylacetamide-diethoxyacetal and the like may also be used in reactions with arylketones (9) to give aminomethylene ketone derivatives (17), (20) and (21). These derivatives are chemical equivalents of hydroxymethyleneketones(α-formylketones) and they react with 3-amino-4-aroylpyrazoles (1) to give 3-aroyl-7-aryl(or heteroaryl)-pyrazolo[1,5-a]pyrimidines as shown in Scheme 3.

The reactions in Scheme 3 illustrate the methods for synthesizing derivatives with an alkyl group at the C-5 position [R_5, formula (23)] or at the C-6 position [R_4, formula (18)] of the pyrazolo[1,5-a]pyrimidine nucleus. This method also allows the preparation of derivatives (22) wherein R_4 and R_5 in formula (13) are both hydrogen. The reaction of ketones (9) and (19) with acetals of N,N-dialkylformamides or acetals of N,N-dialkylacetamides can be carried out in inert solvents or without a solvent.

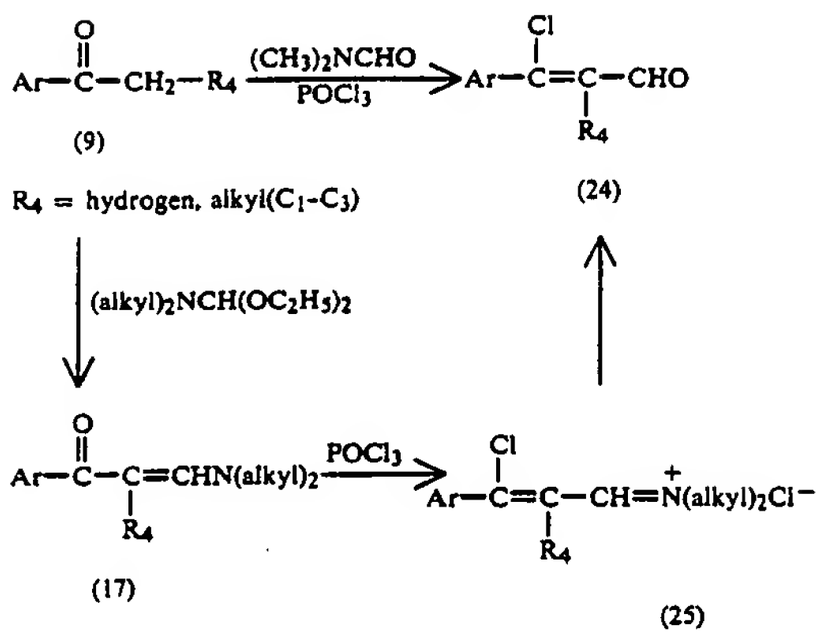
Scheme 3



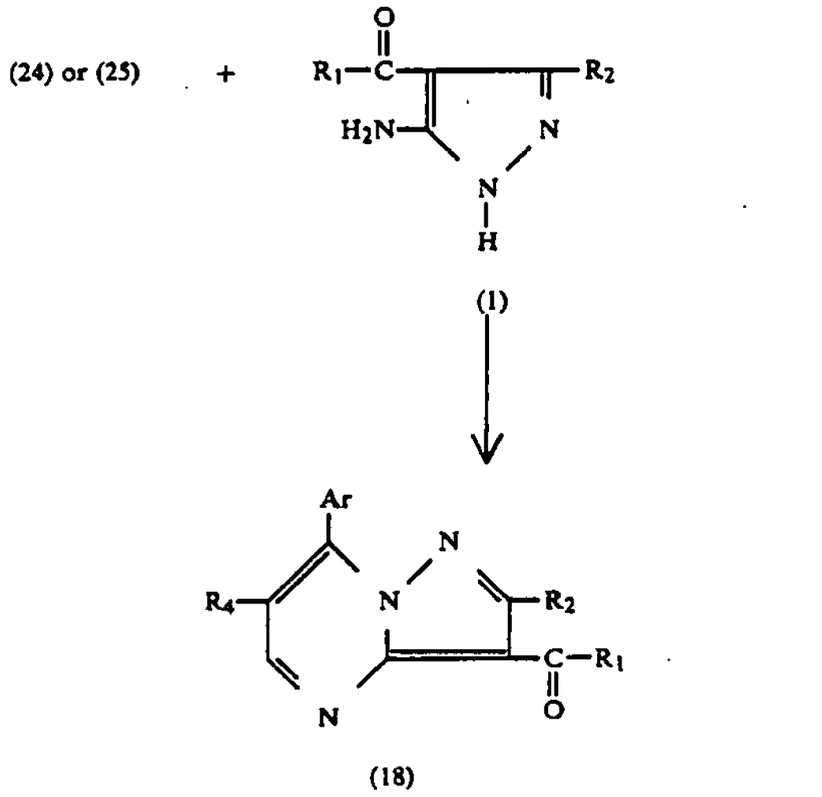
3-Aryl-3-chloroacroleins (24) may also be used as intermediates for the condensation of 3-amino-4-aroyl(or heteroaroyl)pyrazoles to give pyrazolo[1,5-a]pyrimidines as described in Scheme 4. The intermediates (24) are synthesized by the reaction of aryl ketones (9) with N,N-dimethylformamide-phosphorus oxychloride (Vilsmeier reagent) as described by J. A. Virgilio and E. Heilweil, Org. Prep., Proced. Int. 14 (1–2), pp 9–20 (1982) and references cited therein, and M. Weissenfels, et al., Z. Chem., 6, 471 (1966).

The reaction involves a formylation of the ketone followed by chlorination of the initially formylated product. Alternatively, reaction of N,N-dialkylaminomethyleneketones (enaminones) (17) with N,N-dimethylformamide-phosphorus oxychloride affords intermediates (25) which give, on hydrolysis, 3-aryl-3-chloroacroleins (24). Substitution of phosphorus oxybromide for phosphorus oxychloride in the reactions of Scheme 4 affords the corresponding 3-aryl-3-bromoacroleins which may also be condensed with 3-amino-4-aroyl(or heteroaroyl)pyrazoles to give pyrazolo[1,5-a]pyrimidines. The intermediates (25) may be reacted with 3-amino-4-aroyl(or heteroaroyl)pyrazoles to afford pyrazolo[1,5-a]pyrimidines (18).

Scheme 4

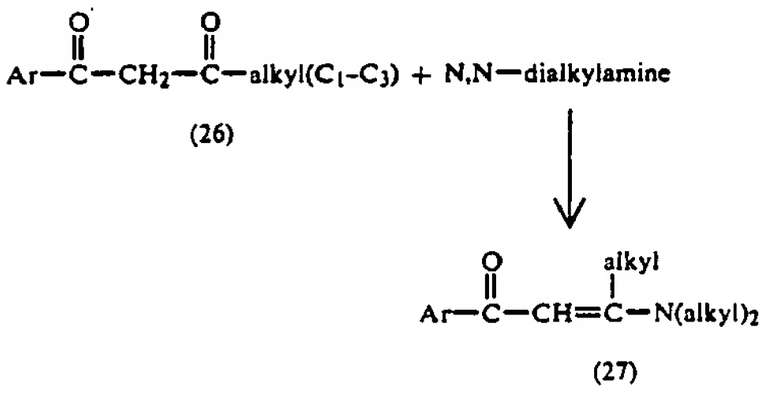


Scheme 5



1-Aryl-1,3-diketones illustrated by structural formula (26) as shown in Scheme 5, react with dialkylamines such as pyrrolidine, dimethylamine, diethylamine and the like to form enaminones (27). Reaction of compounds of structure type (27) with 3-amino-4-aroylpyrazoles (1) under acidic reaction conditions gives pyrazolo[1,5-a]pyrimidines (28).

Scheme 5



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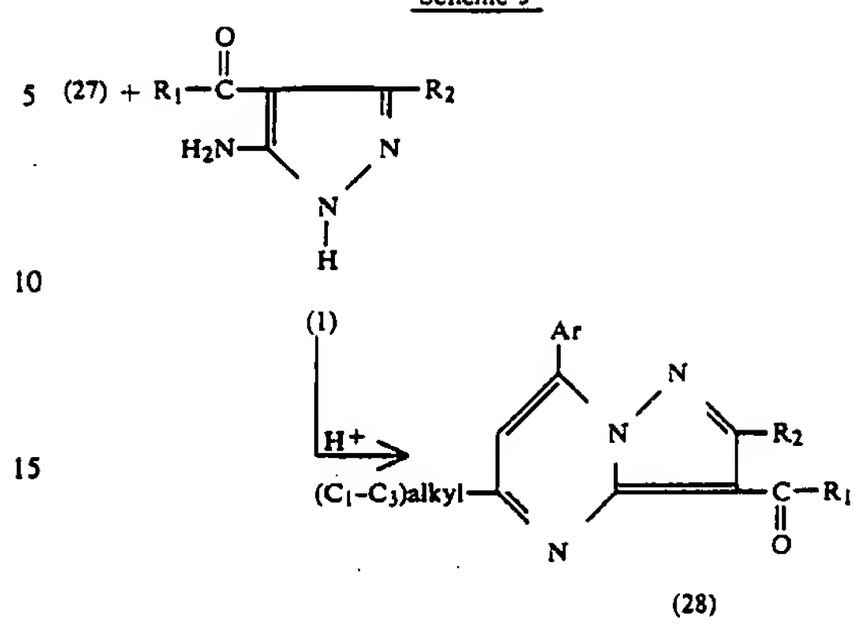
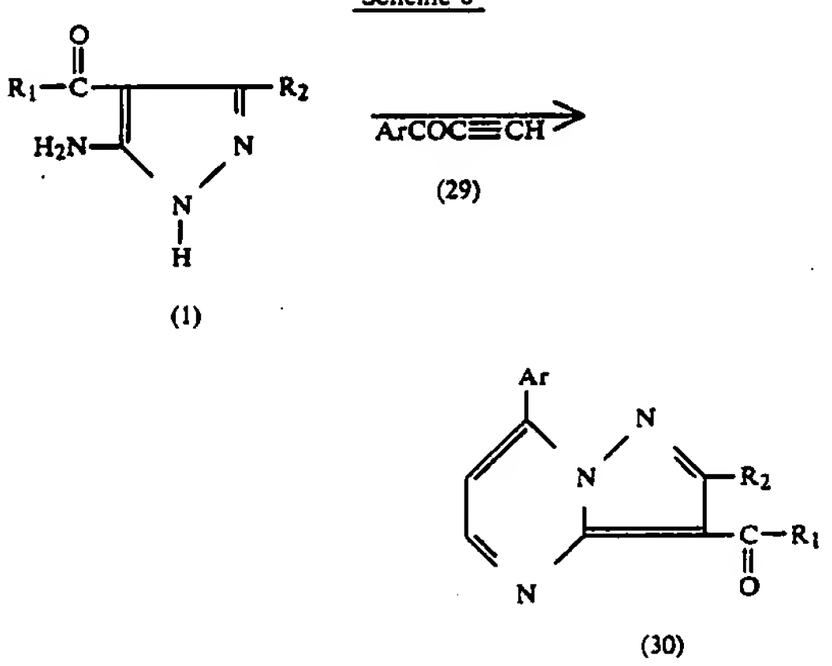
Scheme 5



1-Aroyl-1-propynones (29) react with 3-amino-4-aroylpyrazoles (1) in alkanols such as methanol, ethanol, propanol, butanol and the like under catalysis with acids such as p-toluenesulfonic acid, acetic acid, boron trifluoride and the like at 50° to 100° C. to give 7-arylpyrazolo[1,5-a]pyrimidines (30) as shown in scheme 6. Other suitable solvents for the reaction are benzene, toluene, xylene, dimethylformamide, dimethylacetamide, tetrahydrofuran, dioxane and the like.

Scheme 6



The preferred reaction conditions for condensation of hydroxymethylene ketones (11), 3-(dialkylamino)-1-aryl(or heteroaryl)-2-propen-1-one (17) and the like with 3-amino-4-aroylpyrazoles (1) are heating at 80°–130° C. in glacial acetic acid for 1–10 hours. Alternatively, the condensation reactions may be carried out with inert cosolvents in the presence of glacial acetic acid. Suitable solvents are dioxane, tetrahydrofuran, toluene, xylene, chloroform, carbon tetrachloride and the like. The novel pyrazolo[1,5-a]pyrimidines of this invention may also be prepared by reaction of 3-amino-4-aroylpyrazoles with an appropriate 3-alkoxy, 3-hydroxy, 3-acetoxy, 3-alkylthio, or 3-benzyloxy-1-(aryl or heteroaryl)-2-propen-1-one in inert organic solvents such as lower alkanols, dioxane, tetrahydrofuran, toluene and the like at the reflux temperature thereof and with or without 1 to 10 equivalents of an acid as cata-

lyst. Suitable acid catalysts are glacial acetic acid, hydrochloric acid, trifluoroacetic acid and the like.

The novel compounds of the present invention possess central nervous system activity at nontoxic doses and as such are useful as anxiolytic agents. That is, they produce certain responses in standard tests with laboratory animals which are known to correlate well with relief of anxiety in man. Furthermore, these compounds have been shown by biological data to be useful as antiepileptic agents, particularly in the treatment of grand mal seizures as well as sedative-hypnotic and skeletal muscle relaxant agents.

The anti-anxiety and anticonvulsant properties of the novel compounds of the present invention have been established in a test which indicates anxiolytic and antiepileptic activity by the measure of protection from convulsions resulting from the administration of pentylenetetrazole. Single or graded dose levels of the test compounds were administered orally or intraperitoneally in a 2% starch vehicle, containing 0.5% v/v polyethylene glycol and one drop of Polysorbate 80 to groups of at least 4 rats. At 30 or 60 minutes, the rats were treated intravenously with pentylenetetrazole at a dose of 23 mg/kg of body weight. This dose is estimated to cause clonic seizures in 99% of unprotected rats. It has been reported [R. T. Hill and D. H. Tedeschi, "Animal Testing and Screening Procedures in Evaluating Psychotropic Drugs" in "An Introduction to Psychopharmacology", Eds. R. R. Rech and K. E. Moore, Raven Press, New York, pp 237–288 (1971)] that there is a high degree of correlation between antagonism of pentylenetetrazole seizures in rats and anti-anxiety or anticonvulsant effects in higher warm-blooded animals. The results of this test on representative compounds of the present invention are shown in Table I.

TABLE I

Protection Against Clonic Seizures Caused by Pentylenetetrazole in Rats

Compound	Dose (mg/kg)	% of Rats Protected
phenyl[7-(3-pyridinyl)pyrazolo[1,5-a]-pyrimidin-3-yl]methanone	25.0	100
(4-fluorophenyl)[7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	25.0	100
phenyl[7-(4-pyridinyl)pyrazolo[1,5-a]-pyrimidin-3-yl]methanone	25.0	100
phenyl[7-[3-(trifluoromethyl)phenyl]-pyrazolo[1,5-a]pyrimidin-3-yl]methanone	25.0	100
(4-fluorophenyl)[7-[3-(trifluoromethyl)-phenyl]pyrazolo[1,5-a]pyrimidin-3-yl]-methanone	12.5	38
(4-fluorophenyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	25.0	63
[7-(3,4-dimethoxyphenyl)-5-methylpyrazolo[1,5-a]pyrimidin-3-yl]methanone	25.0	25
[7-(3,4-dimethoxyphenyl)-5-methylpyrazolo[1,5-a]pyrimidin-3-yl](4-fluorophenyl)methanone	25.0	25
2-thienyl[7-[3-(trifluoromethyl)phenyl]-pyrazolo[1,5-a]pyrimidin-3-yl]methanone	25.0	100
2-furanyl[7-(4-pyridinyl)pyrazolo [1,5-a]pyrimidin-3-yl]methanone	25.0	25
[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]-2-thienyl-methanone	25.0	75
2-furanyl[7-[3-(trifluoromethyl)phenyl]-pyrazolo[1,5-a]pyrimidin-3-yl]methanone	25.0	100
2-furanyl[7-(3-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl]methanone	25.0	100
[2-methyl-7-(3-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl]phenyl-methanone	25.0	50
[7-(3,4-dichlorophenyl)-5-methylpyrazolo[1,5-a]pyrimidin-3-yl]phenyl-methanone	25.0	25
(4-methylphenyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	25.0	100
(4-methylphenyl)[7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	25.0	50

TABLE I-continued

Protection Against Clonic Seizures Caused by Pentylenetetrazole in Rats

Compound	Dose (mg/kg)	% of Rats Protected
(4-methylphenyl)[7-[3-(trifluoromethyl)-phenyl]pyrazolo[1,5-a]pyrimidin-3-yl]-methanone	25.0	50
phenyl[7-(4-pyridinyl)pyrazolo[1,5-a]-pyrimidin-3-yl]methanone, pyridine-1-oxide	25.0	100
2-pyridinyl[7-(3-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl]methanone	25.0	75
2-pyridinyl[7-[3-(trifluoromethyl)-phenyl]pyrazolo[1,5-a]pyrimidin-3-yl]-methanone	25.0	100
2-pyridinyl[7-(4-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl]methanone	25.0	100
(3-fluorophenyl)[7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	25.0	100
[7-(4-fluorophenyl)pyrazolo[1,5-a]-pyrimidin-3-yl]phenyl-methanone	25.0	100
[7-(3,5-dichlorophenyl)pyrazolo[1,5-a]-pyrimidin-3-yl]phenyl-methanone	25.0	25
(3-fluorophenyl)[7-(3-pyridinyl)pyrazolo)[1,5-a]pyrimidin-3-yl]methanone	25.0	100
(4-fluorophenyl)[7-(2-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	25.0	50
(2-chlorophenyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	25.0	100
(4-fluorophenyl)[7-(2-fluorophenyl)-pyrazolo[1,5-a]pyrimidin-3-yl]methanone	25.0	50
(4-fluorophenyl)[5-methyl-7-[3-(trifluoromethyl)phenyl]pyrazolo[1,5-a]-pyrimidin-3-yl]methanone	25.0	25
(4-fluorophenyl)[7-[4-(trifluoromethyl)-phenyl]pyrazolo[1,5-a]pyrimidin-3-yl]-methanone	25.0	50
4-[3-(4-fluorobenzoyl)pyrazolo[1,5-a]-pyrimidin-7-yl]benzonitrile	25.0	50
[7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl](3,4,5-trimethoxyphenyl)-methanone	25.0	25
[6-methyl-7-(4-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl]phenyl-methanone	25.0	100
(6-methyl-7-phenylpyrazolo[1,5-a]-pyrimidin-3-yl)phenyl-methanone	25.0	25
3-furanyl[7-(3-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl)methanone	25.0	100
[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl](3,4,5-trimethoxyphenyl)-methanone	25.0	25
(3,4-dimethoxyphenyl)[7-(3-pyridinyl)-pyrazolo[1,5-a]pyrimidin-3-yl]methanone	25.0	87
(3,4-dimethoxyphenyl)[7-[3-(trifluoromethyl)phenyl]pyrazolo[1,5-a]pyrimidin-3-yl]methanone	25.0	50
(3,4-dimethoxyphenyl)[7-(3,4,5-trimethoxyphenyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	25.0	75
(3-methylphenyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	25.0	100
(3,4-dimethoxyphenyl)[7-(4-pyridinyl)-pyrazolo[1,5-a]pyrimidin-3-yl]methanone	25.0	50
(3-methylphenyl)[7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	25.0	100
(3-methylphenyl)[7-[3-(trifluoromethyl)-phenyl]pyrazolo[1,5-a]pyrimidin-3-yl]-methanone	25.0	25
(3-methylphenyl)[7-(3-methylphenyl)-pyrazolo[1,5-a]pyrimidin-3-yl]methanone	25.0	25
(4-chlorophenyl)[5-methyl-7-[3-(trifluoromethyl)phenyl]pyrazolo[1,5-a]-pyrimidin-3-yl]methanone	25.0	25
[5-methyl-7-(4-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl]phenyl-methanone, pyridine-1-oxide	25.0	25
[7-(4-fluorophenyl)pyrazolo[1,5-a]-pyrimidin-3-yl]-2-pyridinyl-methanone	25.0	50
(4-fluorophenyl)[7-(4-fluorophenyl)-pyrazolo[1,5-a]pyrimidin-3-yl]methanone	25.0	75

TABLE I-continued

Compound	Protection Against Clonic Seizures Caused by Pentylenetetrazole in Rats: Dose (mg/kg)	% of Rats Protected
(4-methoxyphenyl)[7-(3-pyridinyl)-pyrazolo[1,5-a]pyrimidin-3-yl]methanone	25.0	100
[7-(4-fluorophenyl)pyrazolo[1,5-a]-pyrimidin-3-yl][3-(trifluoromethyl)-phenyl]methanone	25.0	25
(4-methoxyphenyl)[7-(4-pyridinyl)pyra-zolo[1,5-a]pyrimidin-3-yl]methanone	25.0	25
(3-methoxyphenyl)[7-(4-pyridinyl)pyra-zolo[1,5-a]pyrimidin-3-yl]methanone	25.0	50
(3-methoxyphenyl)[7-(3-pyridinyl)pyra-zolo[1,5-a]pyrimidin-3-yl]methanone	25.0	75
[4-(trifluoromethyl)phenyl][7-[4-(tri-fluoromethyl)phenyl]pyrazolo[1,5-a]-pyrimidin-3-yl]methanone	25.0	25
(3-chlorophenyl)[7-(4-pyridinyl)pyra-zolo[1,5-a]pyrimidin-3-yl]methanone	25.0	50
(3-chlorophenyl)[7-(3-pyridinyl)pyra-zolo[1,5-a]pyrimidin-3-yl]methanone	25.0	50
[7-(3,4-dichlorophenyl)pyrazolo-[1,5-a]pyrimidin-3-yl] [4-(trifluoro-methyl)phenyl]methanone	25.0	50
(4-fluorophenyl)[6-methyl-7-(3-pyri-dinyl)pyrazolo[1,5-a]pyrimidin-3-yl]-methanone	25.0	75
(3-chlorophenyl)[7-(4-fluorophenyl)-pyrazolo[1,5-a]pyrimidin-3-yl]-methanone	25.0	25
(2,5-dichlorophenyl)[7-(4-fluorophen-yl)pyrazolo[1,5-a]pyrimidin-3-yl]-methanone	25.0	25
(2,5-dichlorophenyl)[7-(3-pyridinyl)-pyrazolo[1,5-a]pyrimidin-3-yl]-methanone	25.0	25
(2,5-dichlorophenyl)[7-(4-pyridinyl)-pyrazolo[1,5-a]pyrimidin-3-yl]-methanone	25.0	25
[7-[4-(methylthio)phenyl]pyrazolo-[1,5-a]pyrimidin-3-yl]phenylmethanone	25.0	50
(2-methylphenyl)[7-(3-pyridinyl)pyra-zolo[1,5-a]pyrimidin-3-yl]methanone	25.0	25
(2-methylphenyl)[7-(4-pyridinyl)pyra-zolo[1,5-a]pyrimidin-3-yl]methanone	25.0	25
(2-chlorophenyl)[7-(4-pyridinyl)pyra-zolo[1,5-a]pyrimidin-3-yl]methanone	25.0	25
(2-methylphenyl)[7-[4-(trifluoro-methyl)phenyl]pyrazolo[1,5-a]pyrimi-din-3-yl]methanone	25.0	25
4-pyridinyl[7-(3-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl]methanone	25.0	100
4-pyridinyl)[7-[3-(trifluoromethyl)-phenyl]pyrazolo[1,5-a]pyrimidin-3-yl]-methanone	25.0	100
[7-(4-fluorophenyl)pyrazolo[1,5-a]-pyrimidin-3-yl]-4-pyridinylmethanone	25.0	75
2-pyridinyl[7-[4-(trifluoromethyl)-phenyl]pyrazolo[1,5-a]pyrimidin-3-yl]-methanone	25.0	25
[4-(dimethylamino)phenyl][7-(3-pyri-dinyl)pyrazolo[1,5-a]pyrimidin-3-yl]-methanone	25.0	100
[4-(dimethylamino phenyl][7-(4-pyri-dinyl)pyrazolo[1,5-a]pyrimidin-3-yl]-methanone	25.0	75
[4-(dimethylamino)phenyl][7-[3-(tri-fluoromethyl)phenyl]pyrazolo[1,5-a]-pyrimidin-3-yl]methanone	25.0	100
[2-methyl-7-(4-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl]phenylmethanone	25.0	25
[6-methyl-7-[3-(trifluoromethyl)-phenyl] pyrazolo[1,5-a]pyrimidin-3-yl]-phenylmethanone	25.0	25
(2-methoxyphenyl)[7-(3-pyridinyl)-pyrazolo[1,5-a]pyrimidin-3-yl]-methanone	25.0	75
1,3-benzodioxol-5-yl[7-(3-pyridinyl)-pyrazolo[1,5-a]pyrimidin-3-yl]-methanone	25.0	50

TABLE I-continued

Compound	Protection Against Clonic Seizures Caused by Pentylenetetrazole in Rats: Dose (mg/kg)	% of Rats Protected
1,3-benzodioxol-5-yl[7-(4-pyridinyl)-pyrazolo[1,5-a]pyrimidin-3-yl]-methanone	25.0	25
(4-ethoxyphenyl)[7-(3-pyridinyl)-pyrazolo[1,5-a]pyrimidin-3-yl]-methanone	25.0	25
2-naphthalenyl[7-(3-pyridinyl)pyra-zolo[1,5-a]pyrimidin-3-yl]methanone	25.0	25
2-thienyl[7-[4-(trifluoromethyl)-phenyl]pyrazolo[1,5-a]pyrimidin-3-yl]-methanone	25.0	25
[7-(3-fluorophenyl)pyrazolo[1,5-a]-pyrimidin-3-yl]-2-thienylmethanone	25.0	25
[7-(4-fluorophenyl)pyrazolo[1,5-a]-pyrimidin-3-yl](2-methoxyphenyl)-methanone	25.0	50
(5-methyl-2-thienyl)[7-(3-pyridinyl)-pyrazolo[1,5-a]pyrimidin-3-yl]-methanone	25.0	25
3-thienyl[7-[3-(trifluoromethyl)-phenyl]pyrazolo[1,5-a]pyrimidin-3-yl]-methanone	25.0	75
[7-(3-pyridinyl)pyrazolo[1,5-a]-pyrimidin-3-yl]-3-thienylmethanone	25.0	50
(4-ethylphenyl)[7-(3-pyridinyl)pyra-zolo[1,5-a]pyrimidin-3-yl]methanone	25.0	100
[7-(4-pyridinyl)pyrazolo[1,5-a]-pyrimidin-3-yl]-3-thienylmethanone	25.0	50
(2-fluorophenyl)[7-(4-pyridinyl)pyra-zolo[1,5-a]pyrimidin-3-yl]methanone	25.0	50
(2-fluorophenyl)[7-(3-pyridinyl)pyra-zolo[1,5-a]pyrimidin-3-yl]methanone	25.0	100
(2-fluorophenyl)[7-[3-(trifluoro-methyl)phenyl]pyrazolo[1,5-a]pyrimi-din-3-yl]methanone	25.0	50
phenyl[7-(3-pyridinyl)pyrazolo[1,5-a]-pyrimidin-3-yl]methanone, pyridine-1-oxide	25.0	25
(4-methoxyphenyl)[7-(3-pyridinyl)-pyrazolo[1,5-a]pyrimidin-3-yl]-methanone, pyridine-1-oxide	25.0	25
[7-[3-(ethylamino)phenyl]pyrazolo-[1,5-a]pyrimidin-3-yl]-2-furanyl-methanone	25.0	100
[7-[3-(ethylamino)phenyl]pyrazolo-[1,5-a]pyrimidin-3-yl]phenylmethanone	25.0	100
N—[3-[3-(2-furanylcarbonyl)pyra-zolo[1,5-a]pyrimidin-7-yl]phenyl]-N—methylpropanamide	6.0	100
N—[3-(3-benzoylpyrazolo[1,5-a]py-rimidin-7-yl)phenyl]-N—methylpro-panamide	0.8	100
N—[3-[3-(2-furanylcarbonyl)pyra-zolo[1,5-a]pyrimidin-7-yl]phenyl]-N—methylacetamide	25.0	100
N—[3-(3-benzoylpyrazolo[1,5-a]py-rimidin-7-yl)phenyl]-N—methylace-tamide	0.8	75
N—[3-(3-benzoylpyrazolo[1,5-a]py-rimidin-7-yl)phenyl]-N—ethylpro-panamide	12.5	100
N—ethyl-N—[3-[3-(2-furanylcarbonyl)-pyrazolo[1,5-a]pyrimidin-7-yl]phen-yl]acetamide	12.5	100
N—[3-(3-benzoylpyrazolo[1,5-a]py-rimidin-7-yl)phenyl]-N—ethylace-tamide	6.2	100

Another test which has been used to assess anti-anxiety effects is a nonconditioned passive avoidance procedure described by [J. R. Vogel, B. Beer and D. E. Clody, "A Simple and Reliable Conflict Procedure for Testing Anti-Anxiety Agents", Psychopharmacologia, 21, 1–7 (1971)]. A conflict situation is induced in rats by a modification of this method.

Groups of 6 naive, Wistar strain rats, weighing 200–240 g each were deprived of water for 48 hours and food for 24 hours. The test compounds were administered in single or graded, oral or intraperitoneal doses, suspended in a 2% starch vehicle containing 0.5% v/v polyethylene glycol and one drop of polysorbate 80. Control animals received the vehicle alone. At 30 to 60 minutes each rat was placed in an individual plexiglass chamber. Water was available ad libitum from a tap located in the rear of the chamber. A 0.7 milliampere DC shocking current was established between the stainless steel grid floor and the tap. After 20 licks of nonshocked drinking, a shock was delivered for 2 seconds and then further shocks were delivered on a ratio of one shock for 2 seconds for every 20 licks. This was continued for a total of 3 minutes. The number of shocks taken by each rat during the 3 minute interval was recorded and compared to a control group. The test compounds are considered active if the number of shocks received by the test group is significantly higher than the control group by the Mann-Witney U test. Results of this test on representative compounds of this invention appear in Table II.

TABLE II

Nonconditioned Passive Avoidance Test in Rats

Compound	Dose mg/kg	Result
phenyl[7-(3-pyridinyl)pyrazolo[1,5-a]-pyrimidin-3-yl]methanone	25.0	Active
(4-fluorophenyl)[7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	25.0	Active
phenyl[7-(4-pyridinyl)pyrazolo[1,5-a]-pyrimidin-3-yl]methanone	25.0	Active
phenyl[7-[3-(trifluoromethyl)phenyl)-pyrazolo[1,5-a]pyrimidin-3-yl]methanone	25.0	Active
(4-fluorophenyl)[7-[3-(trifluoromethyl)-phenyl]pyrazolo[1,5-a]pyrimidin-3-yl]-methanone	25.0	Active
(4-fluorophenyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	25.0	Active
[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl][3-(trifluoromethyl)phenyl]-methanone	25.0	Active
2-thienyl[7-[3-(trifluoromethyl)phenyl]-pyrazolo[1,5-a]pyrimidin-3-yl]methanone	25.0	Active
2-furanyl[7-(4-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl]methanone	25.0	Active
2-furanyl[7-[3-(trifluoromethyl)phenyl]-pyrazolo[1,5-a]pyrimidin-3-yl]methanone	25.0	Active
2-furanyl[7-(3-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl]methanone	25.0	Active
4-pyridinyl[7-(4-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl]methanone	25.0	Active
4-methylphenyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	25.0	Active
4-methylphenyl)[7-[3-(trifluoromethyl)-phenyl]pyrazolo[1,5-a]pyrimidin-3-yl] methanone	12.5	Active
phenyl[7-(4-pyridinyl)pyrazolo[1,5-a]-pyrimidin-3-yl]methanone, pyridine-1-oxide	25.0	Active
2-pyridinyl[7-(3-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl]methanone	25.0	Active
2-pyridinyl[7-[3-(trifluoromethyl)-phenyl]pyrazolo[1,5-a]pyrimidin-3-yl]-methanone	25.0	Active
2-pyridinyl[7-(4-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl]methanone	25.0	Active
3-fluorophenyl)[7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	25.0	Active
[7-(4-fluorophenyl)pyrazolo[1,5-a]-pyrimidin-3-yl]phenyl-methanone	25.0	Active
(3-fluorophenyl)[7-(3-pyridinyl)pyrazolo)[1,5-a]pyrimidin-3-yl]methanone	25.0	Active
(2-chlorophenyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	25.0	Active
[6-methyl-7-(4-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl]phenyl-methanone	25.0	Active
3-furanyl[7-(3-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl)methanone	25.0	Active
4-pyridinyl[7-(3-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl]methanone	25.0	Active
(3-methoxyphenyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	25.0	Active
4-pyridinyl[7-[3-(trifluoromethyl)-phenyl]pyrazolo[1,5-a]pyrimidin-3-yl]-methanone	25.0	Active
[4-(dimethylamino)phenyl][7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]-methanone	25.0	Active
[4-(dimethylamino)phenyl][7-[3-(trifluoromethyl)phenyl]pyrazolo[1,5-a]-pyrimidin-3-yl]methanone	25.0	Active
1,3-benzodioxol-5-yl[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	25.0	Active
[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]-3-thienylmethanone	25.0	Active
(4-ethylphenyl)[7-(3-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl]methanone	25.0	Active
(2-fluorophenyl)[7-(4-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl]methanone	25.0	Active
(2-fluorophenyl)[7-(3-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl]methanone	25.0	Active
(2-fluorophenyl)[7-[3-(trifluoromethyl)-phenyl]pyrazolo[1,5-a]pyrimidin-3-yl]-methanone	25.0	Active
[7-[3-(ethylamino)phenyl]pyrazolo[1,5-a]-pyrimidin-3-yl]-2-furanylmethanone	25.0	Active
[7-[3-(ethylamino)phenyl]pyrazolo[1,5-a]-pyrimidin-3-yl] phenylmethanone	25.0	Active
(3,4-dimethoxyphenyl)[7-(3-pyridinyl)-pyrazolo[1,5-a]pyrimidin-3-yl]methanone	25.0	Active
(3-methylphenyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	25.0	Active
(4-chlorophenyl)[7-[3-(trifluoromethyl)-phenyl]pyrazolo[1,5-a]pyrimidin-3-yl]-methanone	25.0	Active
[7-(4-fluorophenyl)pyrazolo[1,5-a]-pyrimidin-3-yl]-2-pyridinyl-methanone	25.0	Active
(4-fluorophenyl)[7-(4-fluorophenyl)-pyrazolo[1,5-a]pyrimidin-3-yl]methanone	25.0	Active
(4-methoxyphenyl)[7-(3-pyridinyl)-pyrazolo[1,5-a]pyrimidin-3-yl]methanone	12.5	Active
N—[3-[3-(2-furanylcarbonyl)pyrazolo-[1,5-a]pyrimidin-7-yl]phenyl]-N—methyl-propanamide	25.0	Active
N—ethyl-N—[3-[3-(2-furanylcarbonyl)py-razolo[1,5-a]pyrimidin-7-yl]phenyl]-propanamide	12.5	Active
N—[4-(3-benzoylpyrazolo[1,5-a]pyrimi-din-7-yl)phenyl]-N—methylacetamide	25.0	Active
N—[3-(3-benzoylpyrazolo[1,5-a]pyrimi-din-7-yl)phenyl]-N—methylpropanamide	1.5	Active
N—[3-[3-(2-furanylcarbonyl)pyrazolo-[1,5-a]pyrimidin-7-yl]phenyl]-N—meth-ylacetamide	25.0	Active
N—[3-(3-benzoylpyrazolo[1,5-a]pyrimi-din-7-yl)phenyl]-N—methylacetamide	3.1	Active
N—[3-(3-benzoylpyrazolo[1,5-a]pyrimi-din-7-yl)phenyl]-N—ethylpropanamide	12.5	Active
N—ethyl-N—[3-[3-(2-furanylcarbonyl)py-razolo[1,5-a]pyrimidin-7-yl]phenyl]-acetamide	12.5	Active
N—[3-(3-benzoylpyrazolo[1,5-a]pyrimi-din-7-yl)phenyl]-N—ethylacetamide	25.0	Active

Another test utilized for the determination of anxiolytic activity is the measurement of the ability of test compounds to inhibit the binding of tritiated benzodiazepines to brain-specific receptors of warm-blooded animals. A modification of the method described by R. F. Squires, et al., Nature, 266, No. 21, p

732 (April, 1977) and H. Mohler, et al., Science, 198, p 849 (1977) was employed.

Male albino rats (Wistar strain, weighing 150–200 g each) were obtained from Royalhart Farms. ^{3}H-Methyldiazepam (79.9 Ci/mmol) and ^{3}H-methyl-flunitrazepam (84.3 Ci/mmol) were obtained from New England Nuclear. The test compounds were solubilized in either dimethylformamide, acetic acid, ethanol or hydrochloric acid.

Whole cortex of rats was homogenized gently in 20 volumes of ice-cold 0.32M sucrose, centrifuged twice at 1000 g for 10 minutes and then recentrifuged at 30,000 g for 20 minutes to produce a crude P_2-synaptosomal fraction. The P_2-fraction was either: (1) resuspended in twice the original volume in hypotonic 50 mM Tris.HCl (pH 7.4), or (2) resuspended in one-half the original volume in hypotonic 10 mM Tris.HCl (pH 7.4) and frozen (−20° C.) until time of use. Frozen P_2 preparations were thawed and resuspended in four times the original homogenizing volume at time of assay.

The binding assay consisted of 300 μl of the P_2-fraction suspension (0.2–0.4 mg protein), 100 μl of test drug and 100 μl of ^{3}H-diazepam (1.5 nM, final concentration) or ^{3}H-flunitrazepam (1.0 nM, final concentration) which was added to 1.5 ml of 50 mM Tris.HCl (pH 7.4). Nonspecific binding controls and total binding controls received 100 μl of diazepam (3 μM, final concentration) and 100 μl of deionized water, respectively, in place of the test compound. Incubation for 30 minutes proceeded in ice and was terminated by filtration, under vacuum, through Whatman GF/C glass fiber filters. The filters were washed twice with 5 ml of ice-cold 50 mM Tris.HCl (pH 7.4) and placed in scintillation vials. After drying at 50°–60° C. for 30 minutes, 10 ml of Beckman Ready-Solv ™ HP (a high performance premix scintillation cocktail, registered trademark of Beckman Instruments, Inc., Irvine, Calif. 92713) was added and the radioactivity determined in a scintillation counter.

Inhibition of binding was calculated by the difference between total binding and binding in the presence of test compound, divided by the total binding, X 100.

The results of this test on representative compounds of the present invention are given in Table III.

TABLE III

Inhibition of the Binding of ^{3}H—Benzodiazepine to Brain-Specific Receptors of Rats

Compound	% Inhibition
phenyl[7-(3-pyridinyl)pyrazolo[1,5-a]-pyrimidin-3-yl]methanone	45
phenyl(7-phenylpyrazolo[1,5-a]pyrimidin-3-yl)methanone	55
phenyl[7-[3-(trifluoromethyl)phenyl]-pyrazolo[1,5-a]pyrimidin-3-yl]methanone	93
(4-fluorophenyl)[7-[3-(trifluoromethyl)-phenyl]pyrazolo[1,5-a]pyrimidin-3-yl]-methanone	50
(4-fluorophenyl)(7-phenylpyrazolo[1,5-a]-pyrimidin-3-yl)methanone	42
[7-(3,4-dimethoxyphenyl)-5-methylpyrazolo-[1,5-a]pyrimidin-3-yl](4-fluorophenyl)-methanone	48
[3-(trifluoromethyl)phenyl][7-[3-(tri-fluoromethyl)phenyl]pyrazolo[1,5-a]-pyrimidin-3-yl]methanone	56
[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl][3-(trifluoromethyl)phenyl]methanone	38
[5-methyl-7-(3-pyridinyl)pyrazolo[1,5-a]-pyrimidin-3-yl]phenyl-methanone	15
phenyl[7-(3,4,5-trimethoxyphenyl)pyrazolo-[1,5-a]pyrimidin-3-yl]methanone	24

TABLE III-continued

Inhibition of the Binding of ^{3}H—Benzodiazepine to Brain-Specific Receptors of Rats

Compound	% Inhibition
2-thienyl[7-[3-(trifluoromethyl)phenyl]-pyrazolo[1,5-a]pyrimidin-3-yl]methanone	99
2-furanyl[7-(4-pyridinyl)pyrazolo[1,5-a]-pyrimidin-3-yl]methanone	19
(7-phenylpyrazolo[1,5-a]pyrimidin-3-yl)-[3-(trifluoromethyl)phenyl]methanone	19
[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]-2-thienyl-methanone	82
[7-(2-furanyl)pyrazolo[1,5-a]pyrimidin-3-yl][3-(trifluoromethyl)phenyl]methanone	36
2-furanyl[7-[3-(trifluoromethyl)phenyl]-pyrazolo[1,5-a]pyrimidin-3-yl]methanone	98
2-furanyl[7-(3-pyridinyl)pyrazolo[1,5-a]-pyrimidin-3-yl]methanone	72
[7-(2-fluorophenyl)pyrazolo[1,5-a]pyrimi-din-3-yl]-2-furanyl-methanone	34
2-furanyl(7-phenylpyrazolo[1,5-a]pyrimi-din-3-yl)methanone	81
[2-methyl-7-(3-pyridinyl)pyrazolo[1,5-a]-pyrimidin-3-yl]phenyl-methanone	52
[7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl][3-(trifluoromethyl)phenyl]methanone	99
4-pyridinyl[7-(4-pyridinyl)pyrazolo[1,5-a]-pyrimidin-3-yl]methanone	11
(2-methyl-7-[3-(trifluoromethyl)phenyl]-pyrazolo[1,5-a]pyrimidin-3-yl)phenyl-methanone	54
[7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]-2-thienyl-methanone	62
phenyl[7-(2-thienyl)pyrazolo[1,5-a]pyrimi-din-3-yl]methanone	96
phenyl[7-(2-pyridinyl)pyrazolo[1,5-a]-pyrimidin-3-yl]methanone	30
[7-(3-chlorophenyl)pyrazolo[1,5-a]pyrimi-din-3-yl]phenyl-methanone	95
[5-methyl-7-(4-pyridinyl)pyrazolo[1,5-a]-pyrimidin-3-yl]phenyl-methanone	93
[7-[2-chloro-5-(trifluoromethyl)phenyl]-pyrazolo[1,5-a]pyrimidin-3-yl]phenyl-methanone	86
[7-(3-fluorophenyl)pyrazolo[1,5-a]pyrimi-din-3-yl]phenyl-methanone	88
phenyl[7-(3-thienyl)pyrazolo[1,5-a]-pyrimidin-3-yl]methanone	96
[7-[3-(methylthio)phenyl]pyrazolo[1,5-a]-pyrimidin-3-yl]phenyl-methanone	98
[7-(3,4-dichlorophenyl)-5-methylpyrazolo-[1,5-a]pyrimidin-3-yl]phenyl-methanone	97
(4-methylphenyl)[7-(3-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl]methanone	56
(4-methylphenyl)[7-(2-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl]methanone	13
(4-methylphenyl)[7-(4-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl]methanone	19
(4-methylphenyl)[7-(3-thienyl)pyrazolo-[1,5-a]pyrimidin-3-yl]methanone	58
phenyl[7-(4-pyridinyl)pyrazolo[1,5-a]-pyrimidin-3-yl]methanone, pyridine-1-oxide	39
2-pyridinyl[7-(3-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl]methanone	98
2-pyridinyl[7-(2-pyridinyl)pyrazolo [1,5-a]pyrimidin-3-yl]methanone	77
2-pyridinyl[7-[3-(trifluoromethyl)phenyl]-pyrazolo[1,5-a]pyrimidin-3-yl]methanone	93
2-pyridinyl[7-(4-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl]methanone	29
(4-fluorophenyl)[7-(4-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl]methanone, pyridine-1-oxide	15
2-pyridinyl[7-(2-thienyl)pyrazolo[1,5-a]-pyrimidin-3-yl]methanone	24
[7-(2,5-dichlorophenyl)pyrazolo[1,5-a]-pyrimidin-3-yl]phenyl-methanone	21
[7-(4-fluorophenyl)pyrazolo[1,5-a]-pyrimidin-3-yl]phenyl-methanone	18
[7-(3,5-dichlorophenyl)pyrazolo[1,5-a]-pyrimidin-3-yl]phenyl-methanone	20
(3-fluorophenyl)[7-(3-pyridinyl)pyrazolo-	20

TABLE III-continued

Inhibition of the Binding of ^3H—Benzodiazepine to Brain-Specific Receptors of Rats	
Compound	% Inhibition
[1,5-a]pyrimidin-3-yl]methanone	
(4-fluorophenyl)[7-(2-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl]methanone	17
(2-chlorophenyl)[7-(3-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl]methanone	24
(4-fluorophenyl)[5-methyl-7-(3-pyridinyl)-pyrazolo[1,5-a]pyrimidin-3-yl]methanone	25
(4-fluorophenyl)[7-(2-fluorophenyl)-pyrazolo[1,5-a]pyrimidin-3-yl]methanone	22
4-(3-benzoylpyrazolo[1,5-a]pyrimidin-7-yl)benzonitrile	10
[5-methyl-7-[3-(trifluoromethyl)phenyl]-pyrazolo[1,5-a]pyrimidin-3-yl]phenyl-methanone	27
[6-methyl-7-(4-pyridinyl)pyrazolo[1,5-a]-pyrimidin-3-yl]phenyl-methanone	56
(6-methyl-7-phenylpyrazolo[1,5-a]pyrimidin-3-yl)phenyl-methanone	24
3-furanyl[7-(3-pyridinyl)pyrazolo[1,5-a]-pyrimidin-3-yl)methanone	77
(3,4-dimethoxyphenyl)[7-(3-pyridinyl)-pyrazolo[1,5-a]pyrimidin-3-yl]methanone	75
(3,4-dimethoxyphenyl)[7-[3-(trifluoro-methyl)phenyl]pyrazolo[1,5-a]pyrimidin-3-yl]methanone	94
(3-methylphenyl)[7-(3-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl]methanone	70
(3,5-dimethoxyphenyl)[7-(3-pyridinyl)-pyrazolo[1,5-a]pyrimidin-3-yl]methanone	30
(3 methylphenyl)[7-[3-(trifluoromethyl)-phenyl]pyrazolo[1,5-a]pyrimidin-3-yl]-methanone	67
(3-methylphenyl)[7-(3-methylphenyl)-pyrazolo[1,5-a]pyrimidin-3-yl]methanone	75
(4-chlorophenyl)[7-[3-(trifluoromethyl)-phenyl]pyrazolo[1,5-a]pyrimidin-3-yl]-methanone	81
(4-chlorophenyl)[7-(3-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl]methanone	87
(4-chlorophenyl)[7-(4-fluorophenyl)-pyrazolo[1,5-a]pyrimidin-3-yl]methanone	16
(3-fluorophenyl)[7-[3-(trifluoromethyl)-phenyl]pyrazolo[1,5-a]pyrimidin-3-yl]-methanone	96
[5-methyl-7-(4-pyridinyl)pyrazolo[1,5-a]-pyrimidin-3-yl]phenyl-methanone, pyridine-1-oxide	52
(3-fluorophenyl)[7-(4-fluorophenyl)pyra-zolo[1,5-a]pyrimidin-3-yl]methanone	52
[7-(4-fluorophenyl)pyrazolo[1,5-a]-pyrimidin-3-yl]-2-pyridinyl-methanone	64
(4-fluorophenyl)[7-(4-fluorophenyl)-pyrazolo[1,5-a]pyrimidin-3-yl]methanone	34
N—[3-(3-benzoylpyrazolo[1,5-a]pyrimidin-7-yl)phenyl]acetamide	65
N—[4-(3-benzoylpyrazolo[1,5-a]pyrimidin-7-yl)phenyl]acetamide	33

The sedative-hypnotic properties of the novel compounds of the instant invention have been established by their effect on the duration of ethanol induced narcosis in rats as a measurement of sedation. Groups of at least 8 rats were administered graded oral doses of the test compounds or vehicle 60 minutes prior to intraperitoneal treatment with 3.2 g/kg ethanol. Rats were then observed continuously for 180 minutes for the incidence and duration of ethanol induced narcosis. A rat was considered to exhibit narcosis if it remained in a supine position on a horizontal surface for at least 1 minute; the end of narcosis was defined as the rat spontaneously righting itself and remaining righted for at least 1 minute. The duration of narcosis was the total time the rat remained in a supine position. The MED [lowest dose necessary to cause a significant ($p \leqq 0.05$, two-tailed Student's t test) increase in the duration of ethanol induced narcosis in rats] of representative compounds of this invention are shown in Table IV. Test compounds were dissolved or suspended in a 2% aqueous starch suspension containing 5% polyethyleneglycol 400 and a drop of Tween ®80; ethanol (95%) was adjusted to final concentration (V:V) with 0.85% saline. All treatments were administered in a constant volume of 5 ml/kg.

TABLE IV

Effects on the Duration of Ethanol Induced Narcosis in Rats	
Compound	MED (mg/kg)
phenyl[7-(3-pyridinyl)pyrazolo[1,5-a]-pyrimidin-3-yl]-methanone	16
(4-fluorophenyl)[7-(4-pyridinyl)-pyrazolo[1,5-a-]pyrimidin-3-yl]-methanone	6
phenyl[7-(4-pyridinyl)pyrazolo[1,5-a]-pyrimidin-3-yl]-methanone	8
2-furanyl[7-[3-(trifluoromethyl)-phenyl]pyrazolo[1,5-a]pyrimidin-3-yl]-methanone	32
2-furanyl[7-(3-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl]-methanone	32
(2-chlorophenyl)[7-(3-pyridinyl)-pyrazolo[1,5-a]pyrimidin-3-yl]-methanone	4

The novel compounds of this invention have also been shown to have skeletal muscle relaxant activity by two tests. The first test measures the effect of representative compounds on the ability of rats to remain on an inclined screen. Groups of at least 6 rats were treated orally with graded doses of test compounds or vehicle and placed on a wire mesh screen (inclined at an angle of 60° from a horizontal level) 65 minutes later. The number of rats falling off the screen within 30 minutes was recorded. The ED_{50}(dose necessary to cause 50% of the animals tested to fall off) was calculated according to the linear arc-sine transformation method of Finney, D. J. Statistical Methods in Biological Assay, 2nd Ed., Hafner, N. Y., 1964, pp. 454 ff. Compounds were dissolved or suspended in a 2% aqueous starch suspension containing 5% polyethylene glycol 400 and a drop of polysorbate 80, and administered in a constant volume of 5 ml/kg. The results of representative compounds of this invention appear in Table V.

TABLE V

Effect on Ability of Rats to Remain on an Inclined Screen	
Compound	ED_{50} (mg/kg)
phenyl[7-(3-pyridinyl)pyrazolo[1,5-a]-pyrimidin-3-yl]-methanone	68.5
(4-fluorophenyl)[7-(4-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl]-methanone	98
phenyl[7-(4-pyridinyl)pyrazolo[1,5-a]-pyrimidin-3-yl]-methanone	9.9
phenyl[7-[3-(trifluoromethyl)phenyl]-pyrazolo[1,5-a]pyrimidin-3-yl]-methanone	5.5
2-furanyl[7-(3-pryidinyl)pyrazolo[1,5-a]-pyrimidin-3-yl]-methanone	167
(4-methylphenyl)[7-(3-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl]-methanone	11.1
2-pyridinyl[7-[3-(trifluoromethyl)-phenyl]pyrazolo[1,5-a]pyrimidin-3-yl]-methanone	6.9
(4-methoxyphenyl)[7-(3-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl]-methanone	11.9

The second test to illustrate that the novel compounds of the present invention possess skeletal muscle

relaxant properties is the effect of representative compounds on the locomotor activity in rats. Groups of 6 rats were treated orally with vehicle (5 ml/kg) or graded doses of the test compounds. Sixty minutes later, individual rats were placed in Actophotometers and locomotor activity was measured for 5 minutes after a brief (30 sec.) habituation period. Motor Activity Counts (number of crossings of the photo cells) were recorded for each rat, and mean activity counts were calculated for each treatment group. The dose causing a 50% decrease in mean activity counts compared with the vehicle group (MDD_{50}) was calculated from a linear regression equation. The test results of representative compounds appear in Table VI.

TABLE VI

Effects on Locomotor Activity in Rats

Compound	MDD_{50} (mg/kg P.O.)
phenyl[7-(3-pyridinyl)pyrazolo[1,5-a]-pyrimidin-3-yl]-methanone	51.4
(4-fluorophenyl)[7-(4-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl]-methanone	48.9
phenyl[7-(4-pyridinyl)pyrazolo[1,5-a]-pyrimidin-3-yl]-methanone	21.2
phenyl[7-[3-(trifluoromethyl)phenyl]-pyrazolo[1,5-a]pyrimidin-3-yl]-methanone	5.5
2-furanyl[7-(3-pyridinyl)pyrazolo[1,5-a]-pyrimidin-3-yl]-methanone	500
(4-methylphenyl)[7-(3-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl]-methanone	13.2
2-pyridinyl[7-[3-(trifluoromethyl)phenyl]-pyrazolo[1,5-a]pyrimidin-3-yl]-methanone	7.0
2-pyridinyl[7-(4-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl]-methanone	100.6
(4-methoxyphenyl)[7-(3-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl]-methanone	10.5

The novel compounds of the present invention have been found to be highly useful for drug therapy in mammals when administered in amounts ranging from about 0.1 mg to about 20.0 mg/kg of body weight per day. A preferred dosage regimen for optimum results would be from about 0.5 mg to about 10.0 mg/kg of body weight per day. Such dosage units are employed that a total of from about 10 to about 700 mg of active compound for a subject of about 70 kg of body weight are administered in a 24 hour period. This dosage regimen may be adjusted to provide the optimum therapeutic response. For example, several divided doses may be administered daily or the dose may be proportionally reduced as indicated by the exigencies of the therapeutic situation. The compounds of this invention are preferably administered orally but may be administered in any convenient manner such as by the intravenous, intramuscular, or subcutaneous routes.

Compositions according to the present invention having the desired clarity, stability and adaptability for parenteral use are obtained by dissolving from 0.10% to 10.0% by weight of active compound in a vehicle consisting of a polyhydric aliphatic alcohol or mixtures thereof. Especially satisfactory are glycerin, propylene glycol, and polyethylene glycols. The polyethylene glycols consist of a mixture of nonvolatile, normally liquid, polyethylene glycols which are soluble in both water and organic liquids and which have molecular weight of from about 200 to 1500. Although the amount of active compound dissolved in the above vehicle may vary from 0.10% to 10.0% by weight, it is preferred that the amount of active compound employed be from about 3.0 to about 9.0% by weight. Although various mixtures of the aforementioned nonvolatile polyethylene glycols may be employed, it is preferred to use a mixture having an average molecular weight of from about 200 to about 400.

In addition to the active compound, the parenteral solutions may also contain various preservatives which may be used to prevent bacterial and fungal contamination. The preservatives which may be used for these purposes are, for example, myristyl-gamma-picolinium chloride, benzalkonium chloride, phenethyl alcohol, p-chlorophenyl-α-glycerol ether, methyl and propyl parabens, and thimerosal. As a practical matter, it is also convenient to employ antioxidants. Suitable antioxidants include, for example, sodium bisulfite, sodium metabisulfite, and sodium formaldehyde sulfoxylate. Generally, from about 0.05 to about 0.2% concentrations of antioxidant are employed.

For intramuscular injection, the preferred concentration of active compound is 0.25 to 0.50 mg/ml of the finished compositions. The novel compounds of the present invention are equally adapted to intravenous administration when diluted with water or diluents employed in intravenous therapy such as isotonic glucose in appropriate quantities. For intravenous use, initial concentrations down to about 0.05 to 0.25 mg/ml of active ingredient are satisfactory.

The active compounds of the present invention may be orally administered, for example, with an inert diluent or with an assimilable edible carrier, or they may be enclosed in hard or soft shell gelatin capsules, or they may be compressed into tablets, or they may be incorporated directly with the food or the diet. For oral therapeutic administration, the active compounds may be incorporated with excipients and used in the form of tablets, troches, capsules, elixirs, suspensions, syrups, wafers, and the like. Additionally, the active ingredient may be incorporated with the proper pharmaceutical carrier or carriers known in the art to produce a sustained-release tablet or capsule. Such compositions and preparations should contain at least 0.1% of active compound. The percentage of the compositions and preparations may, of course, be varied and may conveniently be between about 2% to about 60% of the weight of the unit. The amount of active compound in such therapeutically useful compositions is such that a suitable dosage will be obtained.

The tablets, troches, pills, capsules and the like may also contain one or more of the following: A binder such as gum tragacanth, acacia, corn starch or gelatin; excipients such as dicalcium phosphate; a disintegrating agent such as corn starch, potato starch, alginic acid and the like; a lubricant such as magnesium stearate; a wetting agent such as sodium lauryl sulfate and a sweetening agent such as sucrose, lactose or saccharin may be added or a flavoring agent such as peppermint, oil of wintergreen, or cherry flavoring. When the dosage unit form is a capsule, it may contain, in addition to materials of the above type, a liquid carrier such as a fatty oil. Various other materials may be present as coatings or to otherwise modify the physical form of the dosage unit. For instance, tablets, pills, or capsules may be coated with shellac, sugar or both. A syrup or elixir may contain the active compound, sucrose as a sweetening agent, methyl and propylparabens as preservatives, a dye and flavoring such as cherry or orange flavor. Of course, any material used in preparing any dosage unit form should be pharmaceutically pure and substantially nontoxic in the amounts employed.

The following non-limiting examples illustrate the preparation of representative compounds of the present invention.

EXAMPLE 1

Phenyl[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone

A reaction mixture of 1.87 g of (3-amino-1H-pyrazol-4-yl)phenyl-methanone and 1.76 g of 3-dimethylamino-1-(3-pyridinyl)-2-propen-1-one in 25 ml of glacial acetic acid was refluxed for 6 hours and then the solvent was removed in vacuo giving a crystalline residue. This residue was partitioned between saturated aqueous sodium bicarbonate and methylene chloride. The organic layer was dried with anhydrous sodium sulfate and then passed through a short pad of hydrous magnesium silicate. The addition of hexane to the refluxing eluate induced crystallization. After cooling, the desired product was collected, giving 2.45 g, mp 202°–203° C.

Following the general procedure of Example 1 and using appropriate substituted pyrazole derivatives and either appropriate substituted 3-dimethyl-1-(aryl)-2-propen(buten)-1-ones or in certain instances other aldehydes or ketones, the products of Examples 2–131, listed in Table VII, were obtained.

TABLE VII

Ex.	Pyrazole	3-Dimethylamino-1-(aryl)-2-propen-1-one	Product	MP °C.
2	(3-amino-1H—pyrazol-4-yl)(4-fluorophenyl)-methanone	3-dimethylamino-1-(4-pyridinyl)-2-propen-1-one	(4-fluorophenyl) [7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	214–216
3	(3-amino-1H—pyrazol-4-yl)phenyl-methanone	3-dimethylamino-1-(4-pyridinyl)-2-propen-1-one	phenyl[7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]-methanone	185–186
4	(3-amino-1H—pyrazol-4-yl)phenyl-methanone	3-dimethylamino-1-(phenyl)-2-propen-1-one	phenyl(7-phenylpyrazolo-[1,5-a]pyrimidin-3-yl)-methanone	163–165
5	(3-amino-1H—pyrazol-4-yl)phenyl-methanone	3-dimethylamino-1-[3-(trifluoromethyl)-phenyl]-2-propen-1-one	phenyl[7-[3-(trifluoromethyl)phenyl]pyrazolo[1,5-a]-pyrimidin-3-yl]methanone	148–150
6	(3-amino-1H—pyrazol-4-yl)(4-fluorophenyl)-methanone	3-dimethylamino-1-[3-(trifluoromethyl)-phenyl]-2-propen-1-one	(4-fluorophenyl)[7-[3-(trifluoromethyl)phenyl]pyrazolo-[1,5-a]pyrimidin-3-yl]methanone	176–177
7	(3-amino-1H—pyrazol-4-yl)(4-fluorophenyl)-methanone	3-dimethylamino-1-(3-pyridinyl)-2-propen-1-one	(4-fluorophenyl[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	235–236
8	(3-amino-1H—pyrazol-4-yl)(4-fluorophenyl)-methanone	3-dimethylamino-1-(phenyl)-2-propen-1-one	(4-fluorophenyl)(7-phenyl-pyrazolo[1,5-a]pyrimidin-3-yl]methanone	166–168
9	(3-amino-1H—pyrazol-4-yl)(4-fluorophenyl)-methanone	1-(3,4-dimethoxyphenyl)-3-dimethylamino-2-buten-1-one	[7-(3,4-dimethoxyphenyl)-5-methylpyrazolo[1,5-a]pyrimidin-3-yl](4-fluorophenyl)-methanone	197–199
10	(3-amino-1H—pyrazol-4-yl)[3-(trifluoromethyl)-phenyl]methanone	3-dimethylamino-1-[3-(trifluoromethyl)phenyl]-2-propen-1-one	[3-(trifluoromethyl)phenyl]-[7-[3-(trifluoromethyl)phenyl]pyrazolo[1,5-a]pyrimidin-3-yl]methanone	157–159
11	(3-amino-1H—pyrazol-4-yl)[3-(trifluoromethyl)-phenyl]methanone	3-dimethylamino-1-(3-pyridinyl)-2-propen-1-one	[7-(3-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl][3-trifluoromethyl)phenyl]-methanone	221–222
12	(3-amino-1H—pyrazol-4-yl)phenyl-methanone	3-dimethylamino-1-(3-pyridinyl)-2-buten-1-one	[5-methyl-7-(3-pyridinyl)-pyrazolo[1,5-a]pyrimidin-3-yl]phenyl-methanone	196–198
13	(3-amino-1H—pyrazol-4-yl)phenyl-methanone	3-dimethylamino-1-(3,4,5-trimethoxyphenyl)-2-propen-1-one	phenyl[7-(3-4,5-trimethoxy-phenyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	162–164
14	(3-amino-1H—pyrazol-4-yl)-2-thienyl-methanone	3-dimethylamino-1-[3-(trifluoromethyl)phenyl]-2-propen-1-one	2-thienyl[7-[3-(trifluoromethyl)phenyl]pyrazolo-[1,5-a]pyrimidin-3-yl]-methanone	140–141
15	(3-amino-1H—pyrazol-4-yl)-2-furanyl-methanone	3-dimethylamino-1-(4-pyridinyl)-2-propen-1-one	2-furanyl[7-(4-pyridinyl)-pyrazolo[1,5-a]pyrimidin-3-yl]methanone	277–278
16	(3-amino-1H—pyrazol-4-yl)[3-(trifluoromethyl)-phenyl]methanone	3-dimethylamino-1-(phenyl)-2-propen-1-one	(7-phenylpyrazolo[1,5-a]-pyrimidin-3-yl)[3-(trifluoromethyl)phenyl]methanone	188–190
17	(3-amino-1H—pyrazol-4-yl)-2-thienyl-methanone	3-dimethylamino-1-(3-pyridinyl)-2-propen-1-one	[7-(3-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl]-2-thienyl-methanone	233–234
18	(3-amino-1H—pyrazol-4-yl)[3-(trifluoromethyl)-phenyl]methanone	3-dimethylamino-1-(2-furanyl)-2-propen-1-one	[7-(2-furanyl)pyrazolo-[1,5-a]pyrimidin-3-yl][3-(trifluoromethyl)phenyl]-methanone	143–145
19	(3-amino-1H—pyrazol-4-yl)-2-furanyl-methanone	3-dimethylamino-1-[3-(trifluoromethyl)-phenyl]-2-propen-1-one	2-furanyl[7-[3-(trifluoro-methyl)phenyl]pyrazolo[1,5-]-pyrimidin-3-yl]methanone	153–155
20	(3-amino-1H—pyrazol-4-yl)-2-furanyl-methanone	3-dimethylamino-1-(3-pyridinyl)-2-propen-1-one	2-furanyl[7-(3-pyridinyl)-pyrazolo[1,5-a]pyrimidin-3-yl]methanone	228–229
21	(3-amino-1H—pyrazol-4-	3-dimethylamino-1-(2-	[7-(2-fluorophenyl)pyrazolo-	180–181

TABLE VII-continued

Ex.	Pyrazole	3-Dimethylamino-1-(aryl)-2-propen-1-one	Product	MP °C.
	yl)-2-furanyl-methanone	fluorophenyl)-2-propen-1-one	[1,5-a]pyrimidin-3-yl]-2-furanyl-methanone	
22	(3-amino-1H—pyrazol-4-yl)-2-furanyl-methanone	3-dimethylamino-1-(phenyl)-2-propen-1-one	2-furanyl(7-phenylpyrazolo-[1,5-a]pyrimidin-3-yl]-methanone	179–180
23	(3-amino-5-methyl-1H—pyrazol-4-yl)phenyl-methanone	3-dimethylamino-1-(3-pyridyl)-2-propen-1-one	[2-methyl-7-(3-pyridinyl)-pyrazolo[1,5-a]pyrimidin-3-yl]phenyl-methanone	193–195
24	(3-amino-1H—pyrazol-4-yl)[3-(trifluoromethyl)-phenyl]methanone	3-dimethylamino-1-(4-pyridinyl)-2-propen-1-one	[7-(4-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl][3-(trifluoromethyl)phenyl] methanone	207–208
25	(3-amino-1H—pyrazol-4-yl)-4-pyridinyl-methanone	3-dimethylamino-1-(4-pyridinyl)-2-propen-1-one	4-pyridinyl[7-(4-pyridinyl)-pyrazolo[1,5-a]pyrimidin-3-yl]methanone	260–262
26	(3-amino-5-methyl-1H—pyrazol-4-yl)phenyl-methanone	3-dimethylamino-1-[3-(trifluoromethyl)-phenyl]-2-propen-1-one	(2-methyl-7-[3-(trifluoro-methyl)phenyl]pyrazolo-[1,5-a]pyrimidin-3-yl)phenyl-methanone	156–158
27	(3-amino-1H—pyrazol-4-yl)-2-thienyl-methanone	3-dimethylamino-1-(4-pyridinyl)-2-propen-1-one	7-(4-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl]-2-thienyl-methanone	248–249
28	(3-amino-1H—pyrazol-4-yl)[3-(trifluoromethyl)-phenyl]methanone	3-dimethylamino-1-(3-chlorophenyl)-2-propen-1-one	[7-(3-chlorophenyl)pyrazolo-[1,5-a]pyrimidin-3-yl][3-(trifluoromethyl)phenyl]-methanone	178–180
29	(3-amino-1H—pyrazol-4-yl)phenyl-methanone	3-dimethylamino-1-(2-thienyl)-2-propen-1-one	phenyl[7-(2-thienyl)pyrazolo-[1,5-a]pyrimidin-3-yl]methanone	180–181
30	(3-amino-1H—pyrazol-4-yl)phenyl-methanone	3-dimethylamino-1-(2-pyridinyl)-2-propen-1-one	phenyl[7-(2-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]-methanone	208–210
31	(3-amino-1H—pyrazol-4-yl)phenyl-methanone	3-dimethylamino-1-(3-chlorophenyl)-2-propen-1-one	[7-(3-chlorophenyl)pyrazolo-[1,5-a]pyrimidin-3-yl]phenyl-methanone	136–138
32	(3-amino-1H—pyrazol-4-yl)phenyl-methanone	3-dimethylamino-1-(4-pyridinyl)-2-buten-1-one	[5-methyl-7-(4-pyridinyl)-pyrazolo[1,5-a]pyrimidin-3-yl]phenyl-methanone	209–210
33	(3-amino-1H—pyrazol-4-yl)phenyl-methanone	3-dimethylamino-1-[2-chloro-5-(trifluoro-methyl)phenyl]-2-propen-1-one	[7-[2-chloro-5-(trifluoro-methyl)phenyl]pyrazolo-[1,5-a]pyrimidin-3-yl]phenyl-methanone	145–147
34	(3-amino-1H—pyrazol-4-yl)phenyl-methanone	3-dimethylamino-1-(3-fluorophenyl)-2-propen-1-one	[7-(3-fluorophenyl)pyrazolo-[1,5-a]pyrimidin-3-yl]phenyl-methanone	199–201
35	(3-amino-1H—pyrazol-4-yl)phenyl-methanone	3-dimethylamino-1-(3-thienyl)-2-propen-1-one	phenyl[7-(3-thienyl)pyrazolo-[1,5-a]pyrimidin-3-yl]methanone	150–152
36	(3-amino-1H—pyrazol-4-yl)phenyl-methanone	3-dimethylamino-1-[3-(methylthio)phenyl]-2-propen-1-one	[7-[3-(methylthio)phenyl]-pyrazolo[1,5-a]pyrimidin-3-yl]phenyl-methanone	126–127
37	(3-amino-1H—pyrazol-4-yl)phenyl-methanone	1-(3,4-dichlorophen-yl)-3-(dimethylamino)-2-buten-1-one	[7-(3,4-dichlorophenyl)-5-methylpyrazolo[1,5-a]pyrimi-din-3-yl]phenyl-methanone	194–196
38	(3-amino-1H—pyrazol-4-yl)(4-methylphenyl)-methanone	3-dimethylamino-1-(3-pyridinyl)-2-propen-1-one	(4-methylphenyl)[7-(3-pyri-dinyl)pyrazolo[1,5-a]pyrimi-din-3-yl]methanone	203–204
39	(3-amino-1H—pyrazol-4-yl)(4-methylphenyl)-methanone	3-dimethylamino-1-(2-pyridinyl)-2-propen-1-one	(4-methylphenyl)[7-(2-pyri-dinyl)pyrazolo[1,5-a]pyrimi-din-3-yl]methanone	188–189
40	(3-amino-1H—pyrazol-4-yl)(4-methylphenyl)-methanone	3-dimethylamino-1-(4-pyridinyl)-2-propen-1-one	(4-methylphenyl)[7-(4-pyri-dinyl)pyrazolo[1,5-a]pyrimi-din-3-yl]methanone	196–197
41	(3-amino-1H—pyrazol-4-yl)(4-methylphenyl)-methanone	3-dimethylamino-1-[3-(trifluoromethyl)-phenyl]-2-propen-1-one	(4-methylphenyl)[7-[3-(tri-fluoromethyl)phenyl]pyrazolo-[1,5-a]pyrimidin-3-yl]-methanone	158–159
42	(3-amino-1H—pyrazol-4-yl)(4-methylphenyl)-methanone	3-dimethylamino-1-(3-thienyl)-2-propen-1-one	(4-methylphenyl)[7-(3-thienyl)pyrazolo[1,5-a]-pyrimidin-3-yl]methanone	168–169
43	(3-amino-1H—pyrazol-4-yl)-2-pyridinyl-methanone	3-dimethylamino-1-(3-pyridinyl)-2-propen-1-one	2-pyridinyl[7-(3-pyridinyl)-pyrazolo[1,5-a]pyrimidin-3-yl]methanone	216–218
44	(3-amino-1H—pyrazol-4-yl)-2-pyridinyl-methanone	3-dimethylamino-1-(2-pyridinyl)-2-propen-1-one	2-pyridinyl[7-(2-pyridinyl)-pyrazolo[1,5-a]pyrimidin-3-yl]methanone	158–160
45	(3-amino-1H-pyrazol-4-yl)-2-pyridinyl-methanone	3-dimethylamino-1-[3-(trifluoromethyl)phen-yl]-2-propen-1-one	2-pyridinyl[7-[3-(trifluoro-methyl)phenyl]pyrazolo-[1,5-a]pyrimidin-3-yl]metha-none	166–167

TABLE VII-continued

Ex.	Pyrazole	3-Dimethylamino-1-(aryl)-2-propen-1-one	Product	MP °C.
46	(3-amino-1H—pyrazol-4-yl)-2-pyridinyl-methanone	3-dimethylamino-1-(4-pyridinyl)-2-propen-1-one	2-pyridinyl[7-(4-pyridinyl)-pyrazolo[1,5-a]pyrimidin-3-yl]methanone	230–232
47	(3-amino-1H—pyrazol-4-yl)-3-fluorophenyl-methanone	3-dimethylamino-1-(4-pyridinyl)-2-propen-1-one	(3-fluorophenyl)[7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	195–196
48	(3-amino-1H—pyrazol-4-yl)-2-pyridinyl-methanone	3-dimethylamino-1-(2-thienyl)-2-propen-1-one	2-pyridinyl[7-(2-thienyl)-pyrazolo[1,5-a]pyrimidin-3-yl]methanone	159–160
49	(3-amino-1H—pyrazol-4-yl)phenyl-methanone	3-dimethylamino-1-(2,5-dichlorophenyl)-2-propen-1-one	[7-(2,5-dichlorophenyl)pyrazolo[1,5-a]pyrimidin-3-yl]-phenyl-methanone	194–195
50	(3-amino-1H—pyrazol-4-yl)phenyl-methanone	3-dimethylamino-1-(4-fluorophenyl)-2-propen-1-one	[7-(4-fluorophenyl)pyrazolo-[1,5-a]pyrimidin-3-yl]phenyl-methanone	187–188
51	(3-amino-1H—pyrazol-4-yl)phenyl-methanone	3-dimethylamino-1-(3,5-dichlorophenyl)-2-propen-1-one	[7-(3,5-dichlorophenyl)pyrazolo[1,5-a]pyrimidin-3-yl]-phenyl-methanone	206–208
52	(3-amino-1H—pyrazol-4-yl)-3-fluorophenyl-methanone	3-dimethylamino-1-(3-pyridinyl)-2-propen-1-one	(3-fluorophenyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	185–186
53	(3-amino-1H—pyrazol-4-yl)(4-fluorophenyl)-methanone	3-dimethylamino-1-(2-pyridinyl)-2-propen-1-one	(4-fluorophenyl)[7-(2-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	213–215
54	(3-amino-1H—pyrazol-4-yl)(2-chlorophenyl)-methanone	3-dimethylamino-1-(3-pyridinyl)-2-propen-1-one	(2-chlorophenyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	143–144
55	(3-amino-1H—pyrazol-4-yl)(4-fluorophenyl)-methanone	3-dimethylamino-1-(3-pyridinyl)-2-buten-1-one	(4-fluorophenyl)[5-methyl-7-(3-pyridinyl)yrazolo[1,5-a]-pyrimidin-3-yl]methanone	256–257
56	(3-amino-1H—pyrazol-4-yl)(4-fluorophenyl)-methanone	3-dimethylamino-1-(2-fluorophenyl)-2-propen-1-one	(4-fluorophenyl)[7-(2-fluorophenyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	176–177
57	(3-amino-1H—pyrazol-4-yl)(4-fluorophenyl)-methanone	3-dimethylamino-1-[3-(trifluoromelthyl)-phenyl]-2-buten-1-one	(4-fluorophenyl)[5-methyl-7-[3-(trifluoromethyl)phenyl]-pyrazolo[1,5-a]pyrimidin-3-yl]methanone	189–190
58	(3-amino-1H—pyrazol-4-yl)(4-fluorophenyl)-methanone	3-dimethylamino-1-[4-(trifluoromethyl)phen-yl]-2-propen-1-one	(4-fluorophenyl)[7-[4-(tri-fluoromethyl)phenyl]pyrazolo-[1,5-a]pyrimidin-3-yl]methanone	187–188
59	(3-amino-1H—pyrazol-4-yl)(4-fluorophenyl)-methanone	3-dimethylamino-1-(4-cyanophenyl)-2-propen-1-one	4-[3-(4-fluorobenzoyl)pyrazolo[1,5-a]pyrimidin-7-yl]-benzonitrile	264–266
60	(3-amino-1H—pyrazol-4-yl)phenyl-methanone	3-dimethylamino-1-(4-cyanophenyl)-2-propen-1-one	4-(3-benzoylpyrazolo[1,5-a]-pyrimidin-7-yl)benzonitrile	210–212
61	(3-amino-1H—pyrazol-4-yl)phenyl-methanone	3-dimethylamino-1-[3-(trifluoromethyl)-phenyl]-2-buten-1-one	[5-methyl-7-[3-(trifluoro-methyl)phenyl]pyrazolo-[1,5-a]pyrimidin-3-yl]-phenyl-methanone	153–154
62	(3-amino-1H—pyrazol-4-yl)(3,4,5-trimethoxy-phenyl)methanone	3-dimethylamino-1-(4-pyridinyl)-2-propen-1-one	[7-(4-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl]-[3,4,5-trimethoxyphenyl]-methanone	210–211
63	(3-amino-1H—pyrazol-4-yl)phenyl-methanone	3-dimethylamino-2-methyl-1-(4-pyridinyl)-2-propen-1-one	[6-methyl-7-(4-pyridinyl)-pyrazolo[1,5-a]pyrimidin-3-yl]phenyl-methanone	210–211
64	(3-amino-1H—pyrazol-4-yl)phenyl-methanone	3-dimethylamino-2-methyl-1-phenyl-2-propen-1-one	(6-methyl-7-phenylpyrazolo-[1,5-a]pyrimidin-3-yl)phenyl-methanone	218–220
65	(3-amino-1H—pyrazol-4-yl)-3-furanyl-methanone	3-dimethylamino-1-(3-pyridinyl)-2-propen-1-one	3-furanyl[7-(3-pyridinyl)-pyrazolo[1,5-a]pyrimidin-3-yl]methanone	236–238
66	(3-amino-1H—pyrazol-4-yl)(3,4,5-trimethoxy-phenyl)methanone	3-dimethylamino-1-(3-pyridinyl)-2-propen-1-one	[7-(3-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl](3,4,5-trimethoxyphenyl)methanone	236–237
67	(3-amino-1H—pyrazol-4-yl)(3,4,5-trimethoxy-phenyl)methanone	3-dimethylamino-1-[3-(trifluoromethyl) phenyl]-2-propen-1-one	[7-[3-(trifluoromethyl)phen-yl]pyrazolo[1,5-a]pyrimidin-3-yl](3,4,5-trimethoxyphen-yl)methanone	203–204
68	(3-amino-1H—pyrazol-4-yl)(3,4-dimethoxyphen-yl)methanone	3-dimethylamino-1-(3-pyridinyl)-2-propen-1-one	(3,4-dimethoxyphenyl)[7-(3-pyridinyl)pyrazolo[1,5-a]-pyrimidin-3-yl]methanone	210–211
69	(3-amino-1H—pyrazol-4-yl)(3,4-dimethoxyphen-yl)methanone	3-dimethylamino-1-[3-(trifluoromethyl)-phenyl]-2-propen-1-one	(3,4-dimethoxyphenyl)[7-(3-(trifluoromethyl)phenyl] pyrazolo[1.5-a]pyrimidin-3-yl]methanone	186–187
70	(3-amino-1H—pyrazol-4-yl)(3,4-dimethoxyphen-	3-dimethylamino-1-(3,4,5-trimethoxyphen-	(3,4-dimethoxyphenyl)[7-(3,4,5-trimethoxyphenyl)pyra-	215–216

TABLE VII-continued

Ex.	Pyrazole	3-Dimethylamino-1-(aryl)-2-propen-1-one	Product	MP °C.
	yl)methanone	yl)-2-propen-1-one	zolo[1,5-a]pyrimidin-3-yl]-methanone	
71	(3-amino-1H—pyrazol-4-yl)(3-methylphenyl)-methanone	3-dimethylamino-1-(3-pyridinyl)-2-propen-1-one	(3-methylphenyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	156–158
72	(3-amino-1H—pyrazol-4-yl)(3,5-dimethoxyphenyl)methanone	3-dimethylamino-1-(3-pyridinyl)-2-propen-1-one	(3,5-dimethoxyphenyl)[7-(3-pyridinyl)pyrazolo[1,5-a]-pyrimidin-3-yl]methanone	207–208
73	(3-amino-1H—pyrazol-4-yl)(3,4-dimethoxyphenyl)methanone	3-dimethylamino-1-(4-pyridinyl)-2-propen-1-one	(3,4-dimethoxyphenyl)[7-(4-pyridinyl)pyrazolo[1,5-a]-pyrimidin-3-yl]methanone	232–234
74	(3-amino-1H—pyrazol-4-yl)(3-methylphenyl)-methanone	3-dimethylamino-1-(4-pyridinyl)-2-propen-1-one	(3-methylphenyl)[7-(4-pyriinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	163–165
75	(3-amino-1H—pyrazol-4-yl)(3-methylphenyl)-methanone	3-dimethylamino-1-[3-(trifluoromethyl)-phenyl]-2-propen-1-one	(3-methylphenyl)[7-[3-(trifluoromethyl)phenyl]pyrazolo-[1,5-a]pyrimidin-3-yl]-methanone	163–164
76	(3-amino-1H—pyrazol-4-yl)(3-methylphenyl)-methanone	3-dimethylamino-1-(3-methylphenyl)-2-propen-1-one	(3-methylphenyl)[7-(3-methylphenyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	111–113
77	(3-amino-1H—pyrazol-4-yl)(4-chlorophenyl)-methanone	3-dimethylamino-1-[3-(trifluoromethyl)-phenyl]-2-propen-1-one	(4-chlorophenyl)[7-[3-(trifluoromethyl)phenyl]pyrazolo-[1,5-a]pyrimidin-3-yl)methanone	183–185
78	(3-amino-1H—pyrazol-4-yl)phenyl-methanone	3-dimethylamino-1-phenyl-2-buten-1-one	(5-methyl-7-phenylpyrazolo-[1,5-a]pyrimidin-3-yl)phenyl-methanone	165–166
79	(3-amino-1H—pyrazol-4-yl)(4-chlorophenyl)-methanone	3-dimethylamino-1-(4-pyridinyl)-2-propen-1-one	(4-chlorophenyl)[7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	250–252
80	(3-amino-1H—pyrazol-4-yl)(4-chlorophenyl)-methanone	3-dimethylamino-1-(3-pyridinyl)-2-propen-1-one	(4-chlorophenyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	255–256
81	(3-amino-1H—pyrazol-4-yl)(4-chlorophenyl)-methanone	1-[3-(trifluoromethyl)phenyl]-3-dimethylamino-2-buten-1-one	(4-chlorophenyl)[5-methyl-7-[3-(trifluoromethyl)phenyl]-pyrazolo[1,5-a]pyrimidin-3-yl]methanone	218–220
82	(3-amino-1H—pyrazol-4-yl)(4-chlorophenyl)-methanone	3-dimethylamino-1-(4-fluorophenyl)-2-propen-1-one	(4-chlorophenyl)[7-(4-fluorophenyl)pyrazolo[1,5-a]-pyrimidin-3-yl]methanone	258–260
83	(3-amino-1H—pyrazol-4-yl)(3-fluorophenyl)-methanone	3-dimethylamino-1-[3-(trifluoromethyl)-phenyl]-2-propen-1-one	(3-fluorophenyl)[7-[3-(trifluoromethyl)phenyl]pyrazolo-[1,5-a]pyrimidin-3-yl]methanone	164–165
84	(3-amino-1H—pyrazol-4-yl)(3-fluorophenyl)-methanone	3-dimethylamino-1-(4-fluorophenyl)-2-propen-1-one	(3-fluorophenyl)[7-(4-fluorophenyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	202–203
85	(3-amino-1H—pyrazol-4-yl)-2-pyridinyl-methanone	3-dimethylamino-1-(4-fluorophenyl)-2-propen-1-one	[7-(4-fluorophenyl)pyrazolo-[1,5-a]pyrimidin-3-yl]-2-pyridinyl-methanone	213–214
86	(3-amino-1H—pyrazol-4-yl)(4-fluorophenyl-methanone	3-dimethylamino-1-(4-fluorophenyl)-2-propen-1-one	(4-fluorophenyl)[7-(4-fluorophenyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	224–225
87	(3-amino-1H—pyrazol-4-yl)(4-methoxyphenyl)-methanone	3-dimethylamino-1-(3-pyridinyl)-2-propen-1-one	(4-methoxyphenyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	193–195
88	(3-amino-1H—pyrazol-4-yl)(4-fluorophenyl)-methanone	3-dimethylamino-1-(4-pyridinyl)-2-buten-1-one	(4-fluorophenyl)[5-methyl-7-(4-pyridinyl)pyrazolo[1,5-a]-pyrimidin-3-yl]methanone	256–258
89	(3-amino-1H—pyrazol-4-yl)[3-(trifluoromethyl)phenyl]methanone	3-dimethylamino-1-(4-fluorophenyl)-2-propen-1-one	[7-(4-fluorophenyl)pyrazolo-[1,5-a]pyrimidin-3-yl][3-(trifluoromethyl)phenyl]methanone	193–194
90	(3-amino-1H—pyrazol-4-yl)(4-methoxyphenyl)-methanone	3-dimethylamino-1-(4-pyridinyl)-2-propen-1-one	(4-methoxyphenyl)[7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	235–236
91	(3-amino-1H—pyrazol-4-yl)(3-methoxyphenyl)-methanone	3-dimethylamino-1-(4-pyridinyl)-2-propen-1-one	(3-methoxyphenyl)[7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	144–146
92	(3-amino-1H—pyrazol-4-yl)(3-methoxyphenyl)-methanone	3-dimethylamino-1-(3-pyridinyl)-2-propen-1-one	(3-methoxyphenyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	166–168
93	(3-amino-1H—pyrazol-4-yl)[4-(trifluoromethyl)phenyl]methanone	3-dimethylamino-1-[4-(trifluoromethyl)phenyl]-2-propen-1-one	[4-(trifluoromethyl)phenyl][7-[4-(trifluoromethyl)phenyl]-pyrazolo[1,5-a]pyrimidin-3-yl]-methanone	Syrup
94	(3-amino-1H—pyrazol-4-yl)(3-chlorophenyl)-methanone	3-dimethylamino-1-(4-pyridinyl)-2-propen-1-one	(3-chlorophenyl)[7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	196–198
95	(3-amino-1H—pyrazol-4-	3-dimethylamino-1-(3-	(3-chlorophenyl)[7-(3-pyridin-	Syrup

TABLE VII-continued

Ex.	Pyrazole	3-Dimethylamino-1-(aryl)-2-propen-1-one	Product	MP °C.
	yl)(3-chlorophenyl)-methanone	pyridinyl)-2-propen-1-one	yl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	
96	(3-amino-1H—pyrazol-4-yl)[4-(trifluoromethyl)phenyl]methanone	3-dimethylamino-1-(3,4-dichlorophenyl)-2-propen-1-one	[7-(3,4-dichlorophenyl)pyrazolo[1,5-a]pyrimidin-3-yl][4-(trifluoromethyl)phenyl]methanone	170–172
97	(3-amino-1H—pyrazol-4-yl)(4-fluorophenyl)-methanone	3-dimethylamino-2-methyl-1-(3-pyridinyl)-2-propen-1-one	(4-fluorophenyl)[6-methyl-7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	182–183
98	(3-amino-1H—pyrazol-4-yl)(3-chlorophenyl)-methanone	3-dimethylamino-1-(4-fluorophenyl)-2-propen-1-one	(3-chlorophenyl)[7-(4-fluorophenyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	198–200
99	(3-amino-1H—pyrazol-4-yl)(2,5-dichlorophenyl)methanone	3-dimethylamino-1-(4-fluorophenyl)-2-propen-1-one	(2,5-dichlorophenyl)[7-(4-fluorophenyl)pyrazolo[1,5-a]-pyrimidin-3-yl]methanone	191–192
100	(3-amino-1H—pyrazol-4-yl)(2,5-dichlorophenyl)methanone	3-dimethylamino-1-(3-pyridinyl)-2-propen-1-one	(2,5-dichlorophenyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	201–203
101	(3-amino-1H—pyrazol-4-yl)(2,5-dichlorophenyl)methanone	3-dimethylamino-1-(4-pyridinyl)-2-propen-1-one	(2,5-dichlorophenyl)[7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	189–190
102	(3-amino-1H—pyrazol-4-yl)phenylmethanone	3-dimethylamino-1-[4-(methylthio)phenyl]-2-propen-1-one	[7-[4-(methylthio)phenyl]pyrazolo[1,5-a]pyrimidin-3-yl]-phenylmethanone	141–142
103	(3-amino-1H—pyrazol-4-yl)(2-methylphenyl)-methanone	3-dimethylamino-1-(3-pyridinyl)-2-propen-1-one	(2-methylphenyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	178–180
104	(3-amino-1H—pyrazol-4-yl)(2-methylphenyl)-methanone	3-dimethylamino-1-(4-pyridinyl)-2-propen-1-one	(2-methylphenyl)[7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	125–126
105	(3-amino-1H—pyrazol-4-yl)(2-chlorophenyl)-methanone	3-dimethylamino-1-(4-pyridinyl)-2-propen-1-one	(2-chlorophenyl)[7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	78–81
106	(3-amino-1H—pyrazol-4-yl)(2-methylphenyl)-methanone	3-dimethylamino-1-[4-(trifluoromethyl)-phenyl]-2-propen-1-one	(2-methylphenyl)[7-(4-trifluoromethyl)phenyl]pyrazolo-[1,5-a]pyrimidin-3-yl]methanone	187–189
107	(3-amino-1H—pyrazol-4-yl)-4-pyridinylmethanone	3-dimethylamino-1-(3-pyridinyl)-2-propen-1-one	4-pyridinyl[7-(3-pyridinyl)-pyrazolo[1,5-a]pyrimidin-3-yl]-methanone	253–255
108	(3-amino-1H—pyrazol-4-yl)-4-pyridinylmethanone	3-dimethylamino-1-[3-(trifluoromethyl)phenyl]-2-propen-1-one	4-pyridinyl[7-[3-trifluoromethyl)phenyl]pyrazolo[1,5-a]-pyrimidin-3-yl]methanone	157–159
109	(3-amino-1H—pyrazol-4-yl)-4-pyridinylmethanone	3-dimethylamino-1-(4-fluorophenyl)-2-propen-1-one	[7-(4-fluorophenyl)pyrazolo-[1,5-a]pyrimidin-3-yl]-4-pyridinylmethanone	263–265
110	(3-amino-1H—pyrazol-4-yl)-2-pyridinylmethanone	3-dimethylamino-1-[4-(trifluoromethyl)-phenyl]-2-propen-1-one	2-pyridinyl[7-[4-(trifluoromethyl)phenyl]pyrazolo[1,5-a]-pyrimidin-3-yl]methanone	217–218
111	(3-amino-1H—pyrazol-4-yl)[4-(dimethylamino)-phenyl]methanone	3-dimethylamino-1-(3-pyridinyl)-2-propen-1-one	[4-(dimethylamino)phenyl][7-(3-pyridinyl)pyrazolo[1,5-a]-pyrimidin-3-yl]methanone	226–228
112	(3-amino-1H—pyrazol-4-yl)[4-(dimethylamino)-phenyl]methanone	3-dimethylamino-1-(4-pyridinyl)-2-propen-1-one	[4-(dimethylamino)phenyl][7-(4-pyridinyl)pyrazolo[1,5-a]-pyrimidin-3-yl]methanone	224–225
113	(3-amino-1H—pyrazol-4-yl)[4-(dimethylamino)-phenyl]methanone	3-dimethylamino-1-[3-(trifluoromethyl)-phenyl]-2-propen-1-one	[4-(dimethylamino)phenyl][7-[3-(trifluoromethyl)phenyl]-pyrazolo[1,5-a]pyrimidin-3-yl]-methanone	153–155
114	(3-amino-5-methyl-1H—pyrazol-4-yl)phenyl-methanone	3-dimethylamino-1-(4-pyridinyl)-2-propen-1-one	[2-methyl-7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]-phenylmethanone	178–180
115	(3-amino-1H—pyrazol-4-yl)phenylmethanone	3-dimethylamino-2-methyl-1-[3-(trifluoromethyl)phenyl]-2-propen-1-one	[6-methyl-7-[3-(trifluoromethyl)phenyl]pyrazolo[1,5-a]-pyrimidin-3-yl]methanone	174–175
116	(3-amino-1H—pyrazol-4-yl)(2-methoxyphenyl)-methanone	3-dimethylamino-1-(3-pyridinyl)-2-propen-1-one	(2-methoxyphenyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	144–145
117	(3-amino-1H—pyrazol-4-yl)[3,4-(methylenedioxy)phenyl]methanone	3-dimethylamino-1-(3-pyridinyl)-2-propen-1-one	1,3-benzodioxol-5-yl[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	212–213
118	(3-amino-1H—pyrazol-4-yl)[3,4-methylenedioxy)phenyl]methanone	3-dimethylamino-1-(4-pyridinyl)-2-propen-1-one	1,3-benzodioxol-5-yl[7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	236–237
119	(3-amino-1H—pyrazol-4-yl)(4-ethoxyphenyl)-methanone	3-dimethylamino-1-(3-pyridinyl)-2-propen-1-one	(4-ethoxyphenyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	193–194
120	(3-amino-1H—pyrazol-4-yl)-2-naphthalenyl-methanone	3-dimethylamino-1-(3-pyridinyl)-2-propen-1-one	2-naphthalenyl[7-(3-pyridinyl)-pyrazolo[1,5-a]pyrimidin-3-yl]-methanone	218–220

TABLE VII-continued

Ex.	Pyrazole	3-Dimethylamino-1-(aryl)-2-propen-1-one	Product	MP °C.
121	(3-amino-1H—pyrazol-4-yl)-2-thienylmethanone	3-dimethylamino-1-[4-(trifluoromethyl)-phenyl]-2-propen-1-one	2-thienyl[7-[4-(trifluoromethyl)phenyl]pyrazolo[1,5-a]-pyrimidin-3-yl]methanone	191–193
122	(3-amino-1H—pyrazol-4-yl)-2-thienylmethanone	3-dimethylamino-1-(3-fluorophenyl)-2-propen-1-one	[7-(3-fluorophenyl)pyrazolo-[1,5-a]pyrimidin-3-yl]-2-thienylmethanone	235–237
123	(3-amino-1H—pyrazol-4-yl)(2-methoxyphenyl)-methanone	3-dimethylamino-1-(4-fluorophenyl)-2-propen-1-one	[7-(4-fluorophenyl)pyrazolo-[1,5-a]pyrimidin-3-yl](2-methoxyphenyl)methanone	193–194
124	(3-amino-1H—pyrazol-4-yl)(5-methyl-2-thienyl)methanone	3-dimethylamino-1-(3-pyridinyl)-2-propen-1-one	(5-methyl-2-thienyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	185–187
125	(3-amino-1H—pyrazol-4-yl)-3-thienylmethanone	3-dimethylamino-1-[3-(trifluoromethyl)-phenyl]-2-propen-1-one	3-thienyl[7-[3-(trifluoromethyl)phenyl]pyrazolo[1,5-a]pyrimidin-3-yl]methanone	124–125
126	(3-amino-1H—pyrazol-4-yl)-3-thienylmethanone	3-dimethylamino-1-(3-pyridinyl)-2-propen-1-one	[7-(3-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl]-3-thienylmethanone	203–204
127	(3-amino-1H—pyrazol-4-yl)(4-ethylphenyl)-methanone	3-dimethylamino-1-(3-pyridinyl)-2-propen-1-one	(4-ethylphenyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	143–144
128	(3-amino-1H—pyrazol-4-yl)-3-thienylmethanone	3-dimethylamino-1-(4-pyridinyl)-2-propen-1-one	[7-(4-pyridinyl)pyrazolo-[1,5-a]pyrimidin-3-yl]-3-thienylmethanone	197–198
129	(3-amino-1H—pyrazol-4-yl)(2-fluorophenyl)-methanone	3-dimethylamino-1-(4-pyridinyl)-2-propen-1-one	(2-fluorophenyl)[7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	188–189
130	(3-amino-1H—pyrazol-4-yl)(2-fluorophenyl)-methanone	3-dimethylamino-1-(3-pyridinyl)-2-propen-1-one	(2-fluorophenyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone	164–165
131	(3-amino-1H—pyrazol-4-yl)(2-fluorophenyl)-methanone	3-dimethylamino-1-[3-(trifluoromethyl)-phenyl]-2-propen-1-one	(2-fluorophenyl)[7-[3-(trifluoromethyl)phenyl]pyrazolo-[1,5-a]pyrimidin-3-yl]methanone	155–157

EXAMPLE 132

Phenyl[7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone, pyridine-1-oxide

A 3.0 g portion of [7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone was dissolved in 200 ml of methylene chloride. A 2.0 g portion of 80–90% m-chloroperbenzoic acid was added and the mixture was stirred for 18 hours. The solid was collected, air dried, slurried in 50 ml of saturated aqueous sodium bicarbonate, added to 150 ml of water and heated to boiling. The solution was clarified while hot, then cooled. The solid was washed with water and air dried at 50° C., giving 0.4 g of the desired product, mp 239°–244° C.

EXAMPLE 133

(4-Fluorophenyl)[7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone, pyridine-1-oxide

A 1.6 g portion of (4-fluorophenyl)[7-(4-pyridinyl)-pyrazolo[1,5-a) pyrimidin-3-yl]methanone was reacted as described in Example 132, giving 1.0 g of the desired product, mp 283°–285° C. (dec.).

EXAMPLE 134

[5-Methyl-7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]phenyl-methanone, pyridine-1-oxide

A 2.1 g portion of [5-methyl-7-(4-pyridinyl)-pyrazolo[1,5-a]pyrimidin-3-yl]phenyl-methanone was reacted as described in Example 132, giving 1.8 g of the desired product, mp 249°–250° C.

EXAMPLE 135

Phenyl(7-phenylpyrazolo[1,5-a]pyrimidin-3-yl)methanone

A mixture of 0.01 mole of 3-chloro-3-phenyl-2-propenal and 0.01 mole of (3-amino-1H-pyrazol-4-yl)phenylmethanone in 25 ml of acetic acid was refluxed for 6 hours. The solvent was removed in vacuo and the product isolated as described in Example 1, giving the desired product as crystals, mp 163°–165° C.

EXAMPLE 136

2-Furanyl[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone

A mixture of 0.02 mole of 3-chloro-3-(3-pyridinyl)-2-propenal and 0.02 mole of (3-amino-1H-pyrazol-4-yl)-2-furanyl-methanone in 30 ml of glacial acetic acid was refluxed for 5 hours. The solvent was removed in vacuo and the residue partitioned between saturated aqueous sodium bicarbonate and dichloromethane. The dichloromethane layer was dried over sodium sulfate and passed through a short pad of hydrous magnesium silicate. The eluent was concentrated and the residue crystallized from dichloromethane:hexane to give the desired product as crystals, mp 228°–229° C.

EXAMPLE 137

2-Furanyl[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone

A mixture of 0.1 mole of 3-dimethylamino-1-(3-pyridinyl)-2-propen-1-one and a 0.15 mole of pyrrolidine in 200 ml of xylene was refluxed with distillation of the xylene by passing a stream of argon through the solution. Additional xylene was added periodically. After 10 hours the solvent was removed to give crude

3-(1-pyrrolidinyl)-1-(3-pyridinyl)-2-propen-1-one. This crude compound and 0.1 mole of (3-amino-1H-pyrazol-4-yl)-2-furanyl-methanone in 100 ml of glacial acetic acid was refluxed for 8 hours. The solvent was removed in vacuo and the product isolated as described in Example 1, giving the desired product as crystals, mp 228°–229° C.

EXAMPLE 138

[5-Methyl-7-[3-(trifluoromethyl)phenyl]pyrazolo[1,5-a]pyrimidin-3-yl]phenyl-methanone

A mixture of 0.05 mole of 1-[3-[3-(trifluoromethyl)-phenyl]butan-1,3-dione and 0.05 mole of (3-amino-1H-pyrazol-4-yl)phenyl-methanone in 40 ml of glacial acetic acid was refluxed for 10 hours. The solvent was removed in vacuo and the residue partitioned between saturated aqueous sodium bicarbonate and dichloromethane. The dichloromethane layer was dried over sodium sulfate and passed through a short pad of hydrous magnesium silicate. The eluent was concentrated and the residue was crystallized from dichloromethane:hexane to give the desired product as crystals, mp 153°–154° C.

EXAMPLE 139

(5-Methyl-7-phenylpyrazolo[1,5-a]pyrimidin-3-yl)phenyl-methanone

A mixture of 0.01 mole of 1-(3-phenyl)butan-1,3-dione and 0.01 mole of (3-amino-1H-pyrazol-4-yl)phenyl-methanone in 25 ml of n-butanol was refluxed for 8 hours. The solvent was removed and the product isolated as described in Example 1, giving the desired product as crystals, mp 165°–166° C.

EXAMPLE 140

[5-Methyl-7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]phenyl-methanone

A mixture of 0.05 mole of 3-(1-pyrrolidinyl)-1-(4-pyridinyl)-2-buten-1-one and 0.05 ml of (3-amino-1H-pyrazol-4-yl)phenyl-methanone in 50 ml of glacial acetic acid was refluxed for 8 hours. The solvent was removed and the residue partitioned between saturated aqueous sodium bicarbonate and dichloromethane. The dichloromethane layer was washed with water, dried over magnesium sulfate and passed through a short pad of hydrous magnesium silicate. The eluent was concentrated and the residue crystallized from dichloromethane:hexane, giving the desired product, mp 209°–210° C.

EXAMPLE 141

Phenyl[7-[(3-trifluoromethyl)phenyl]pyrazolo[1,5-a]pyrimidin-3-yl]methanone

A mixture of 100 ml of diethyl ether, 3.36 g of sodium hydride (60% in oil), 7.4 g of ethyl formate and 18.8 g of m-trifluoromethylacetophenone was refluxed with vigorous stirring for 2 hours, then cooled and the precipitate collected, giving 14.6 g of the sodium salt of 3-hydroxy-3-(trifluoromethyl)acrylophenone.

A suspension of 12.0 g of the above compound in 75 ml of dioxane and 10 ml of acetic anhydride was stirred at room temperature for 2 hours and then poured into water. The precipitate was collected, dissolved in dichloromethane and passed through a short pad of hydrous magnesium silicate. The eluent was concentrated and hexane added, giving 3-hydroxy-3'-(trifluoromethyl)acrylophenone acetate as crystals, mp 55°–57° C. A mixture of 0.03 mole of these crystals and 0.03 mole of (3-amino-1H-pyrazol-4-yl)phenyl-methanone in 30 ml of glacial acetic acid was refluxed for 5 hours. The solvent was removed and the residue partitioned between saturated aqueous sodium bicarbonate and dichloromethane. The dichloromethane layer was dried over magnesium sulfate and passed through a short pad of hydrous magnesium silicate. The eluent was concentrated and diluted with hexane, giving the desired product as crystals, mp 148°–150° C.

EXAMPLE 142

Phenyl[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone

A mixture of 0.02 mole of 3-chloro-3-(3-pyridinyl)-2-propenal and 0.02 mole of (3-amino-1H-pyrazol-4-yl)phenyl-methanone in 25 ml of glacial acetic acid was refluxed for 5 hours. The solvent was removed and the product isolated as described in Example 1, giving the desired product as crystals, mp 202°–203° C.

EXAMPLE 143

Phenyl(7-phenylpyrazolo[1,5-a]pyrimidin-3-yl)methanone

A mixture of 3.2 g (0.02 mole) of 3-chloro-3-phenyl-2-propenal and 0.02 mole of (3-amino-1H-pyrazol-4-yl)phenyl-methanone in 25 ml of glacial acetic acid was refluxed for 6 hours. The solvent was removed and the product was isolated as described in Example 1, giving crystals, mp 163°–165° C.

EXAMPLE 144

[5-Methyl-7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]phenyl-methanone

A mixture of 8.16 g (0.05 mole) of 1-(3-pyridinyl)butan-1,3-dione and 0.05 mole of (3-amino-1H-pyrazol-4-yl)phenyl-methanone in 40 ml of glacial acetic acid was refluxed for 8 hours. The solvent was removed in vacuo and the product isolated as described in Example 1, giving the desired product as crystals, mp 196°–198° C.

EXAMPLE 145

[5-Methyl-7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]phenyl-methanone

A mixture of 8.16 g (0.05 mole) of 1-(3-pyridinyl)butan-1,3-dione and 0.05 mole of (3-amino-1H-pyrazol-4-yl)phenyl-methanone in xylene was refluxed for 20 hours. The solvent was removed and the residue dissolved in dichloromethane. This solution was filtered, dried over magnesium sulfate and passed through a short pad of hydrous magnesium silicate. The eluent was concentrated with hexane added during concentration. Cooling and filtration gave the desired product as crystals, mp 196°–198° C.

EXAMPLE 146

[5-Methyl-7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]phenyl-methanone

To a solution of 16.32 g of 1-(3-pyridinyl)butan-1,3-dione in 200 ml of ethyl acetate was added 7.11 g of pyrrolidone. The mixture was stirred at room temperature and then the crystals were collected giving 7.0 g of 3-(1-pyrrolidinyl)-1-(3-pyridinyl)-2-buten-1-one, mp 116°–118° C.

A 0.02 mole portion of the above compound and 0.02 mole of (3-amino-1H-pyrazol-4-yl)phenyl-methanone in 25 ml of glacial acetic acid was refluxed for 8 hours. The solvent was removed and the product isolated as described in Example 1, giving the desired product as crystals, mp 196°–198° C.

EXAMPLE 147

Phenyl[7-[(3-trifluoromethyl)phenyl]pyrazolo[1,5-a]pyrimidin-3-yl]methanone

A mixture of 0.10 mole of 3-dimethylamino-1-[(3-trifluoromethyl)phenyl]-2-propen-1-one and 0.10 mole of p-toluenesulfonic acid in 100 ml of ethanol was warmed at 60° C. for 12 hours and the solvent removed in vacuo. The residue was partitioned between dichloromethane and water. The organic layer was dried over magnesium sulfate and concentrated, giving crude 3-ethoxy-1-[(3-trifluoromethyl)phenyl]-2-propen-1-one.

A mixture of the above compound and 0.10 mole of (3-amino-1H-pyrazol-4-yl)phenyl-methanone in 75 ml of glacial acetic acid was refluxed for 5 hours. The solvent was removed and the product isolated as described in Example 1, giving the desired product as crystals, mp 148°–150° C.

EXAMPLE 148

Phenyl[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone

A mixture of 0.02 mole of 3-ethoxy-1-(3-pyridinyl)-2-propen-1-one, 0.02 mole of (3-amino-1H-pyrazol-4-yl)phenyl-methanone and 100 ml of xylene was refluxed for 12 hours. The solvent was removed and the residue dissolved in dichloromethane. This solution was dried over sodium sulfate and the product isolated as described in Example 1, as crystals, mp 202°–203° C.

EXAMPLE 149

2-Pyridinyl[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone

A mixture of 0.10 mole of 3-dimethylamino-1-(3-pyridinyl)-2-propen-1-one and 0.20 mole of p-toluenesulfonic acid in 150 ml of anhydrous ethanol was refluxed for 10 hours. The solvent was removed and the residue partitioned between water and dichloromethane. The organic layer was dried over magnesium sulfate and the solvent removed, giving 3-ethoxy-1-(3-pyridinyl)-2-propen-1-one.

The above compound was reacted with (3-amino-1H-pyrazol-4-yl)-2-pyridinyl-methanone in acetic acid as described in Example 1, giving the desired product as crystals, mp 216°–218° C.

EXAMPLE 150

(4-Methylphenyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone

A mixture of 0.10 mole of 3-acetylpyridine and 0.10 mole of N,N-dimethylformamide dimethylacetal in 100 ml of benzene was refluxed for 12 hours. The solvent was removed, giving 3-dibutylamino-1-(3-pyridinyl)-2-propen-1-one.

The above compound was reacted with (3-amino-1H-pyrazol-4-yl) (4-methylphenyl)methanone in glacial acetic acid as described in Example 1, giving the desired product as crystals, mp 203°–204° C.

EXAMPLE 151

(4-Methoxyphenyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone

A mixture of 0.10 mole of 3-acetylpyridine and 0.10 mole of N,N-diethylformamide dimethylacetal in 100 ml of dioxane was refluxed for 10 hours. The solvent was removed, giving 3-diethylamino-1-(3-pyridinyl)-2-propen-1-one.

A mixture of 0.10 mole of the above compound and 0.10 mole of (3-amino-1H-pyrazol-4-yl) (4-methoxyphenyl)methanone in glacial acetic acid was refluxed for 6 hours. The product was isolated as described in Example 1, giving crystals, mp 193°–195° C.

EXAMPLE 152

2-pyridinyl[7-[3-(trifluoromethyl)phenyl]pyrazolo[1,5-a]pyrimidin-3-yl]methanone

A mixture of 0.10 mole of 3-acetylpyridine and 0.10 mole of N,N-dimethylformamide dicyclohexylacetal in 100 ml of dioxane was refluxed for 8 hours. The solvent was removed in vacuo, giving 3-dimethylamino-1-[3-(trifluoromethyl)phenyl]-2-propen-1-one. The above compound was reacted with (3-amino-1H-pyrazol-4-yl)-2-pyridinyl-methanone as described in Example 1, giving the desired product as crystals, mp 166°–167° C.

EXAMPLE 153

2-Pyridinyl[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidinyl-3-yl]methanone

A mixture of 25 g of 3-acetylpyridine and 35 ml of N,N-dimethylformamide dipropylacetal was heated at 100° C. for 6 hours. The mixture was concentrated in vacuo and the residue crystallized, giving 3-dimethylamino-1-(3-pyridinyl)-2-propen-1-one.

The above compound was reacted with (3-amino-1H-pyrazol-4-yl)-2-pyridinyl-methanone as described in Example 1, giving the desired product as crystals, mp 216°–218° C.

EXAMPLE 154

(4-Methylphenyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone

To a mixture of 0.10 mole of 3-acetylpyridine in 100 ml of tetrahydrofuran was added 0.10 mole of tert.-butoxy-bis-(dimethylamino)methane. The mixture was stirred for 24 hours and the solvent removed, giving 3-dimethylamino-1-(3-pyridinyl)-2-propen-1-one.

The above compound was reacted with (3-amino-1H-pyrazol-4-yl) (4-methylphenyl)methanone as described in Example 1, giving the desired product as crystals, mp 203°–204° C.

EXAMPLE 155

2-Furanyl[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone

A mixture of 0.02 mole of 3-acetylpyridine and 0.022 mole of tris(dimethylamino)methane in benzene was refluxed for 5 hours, giving 3-dimethylamino-1-(3-pyridinyl)-2-propen-1-one.

The above compound was reacted with (3-amino-1H-pyrazol-4-yl)-2-furanyl-methanone as described in Example 1, giving the desired product as crystals, mp 228°–229° C.

EXAMPLE 156

Phenyl-[7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone

A mixture of 0.10 mole of 4-acetylpyridine and 40 ml of N,N-dimethylformamide diethylacetal was refluxed for 5 hours. The mixture was concentrated in vacuo, giving 3-dmethylamino-1-(4-pyridinyl)-2-propen-1-one.

The above compound (0.05 mole) and 0.05 mole of (3-amino-1H-pyrazol-4-yl)phenyl-methanone were reacted as described in Example 1, giving the desired product as crystals, mp 185°–186° C.

EXAMPLE 157

Phenyl[7-[(3-trifluoromethyl)phenyl]pyrazolo[1,5-a]pyrimidin-3-yl]methanone

A mixture of 0.10 mole of m-trifluoromethylacetophenone and 100 ml of N,N-dimethylformamide dibutylacetal was heated to 100° C. for 10 hours. The mixture was concentrated in vacuo and the residue crystallized, giving 3-dimethylamino-1-[(3-trifluoromethyl)phenyl]-2-propen-1-one.

A 0.05 mole portion of the above compound was reacted with 0.05 mole of (3-amino-1H-pyrazol-4-yl)phenylmethanone as described in Example 1, giving the desired product as crystals, mp 148°–150° C.

EXAMPLE 158

(4-Fluorophenyl)[7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone

A mixture of 0.10 mole of 4-acetylpyridine and 0.12 mole of N,N-dimethylformamide dibenzylacetal in benzene was refluxed for 8 hours, giving 3-dimethylamino-1-(4-pyridinyl)-2-propen-1-one.

A 0.05 mole portion of the above compound and 0.05 mole of (3-amino-1H-pyrazol-4-yl)(4-fluorophenyl)methanone were reacted as described in Example 1, giving the desired product as crystals, mp 214°–216° C.

EXAMPLE 159

[7-(3-Pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]-2-thiazolyl-methanone

As described for Example 1, (3-amino-1H-pyrazol-4-yl)-2-thiazolyl-methanone was reacted with 3-dimethylamino-1-(3-pyridinyl)-2-propen-1-one to give the product as colorless crystals, mp 262°–264° C.

EXAMPLE 160

[7-(4-Pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]-2-thiazolyl-methanone

As described for Example 1, (3-amino-1H-pyrazol-4-yl)-2-thiazolyl-methanone was reacted with 3-dimethylamino-1-(4-pyridinyl)-2-propen-1-one to give the product as crystals, mp 323°–325° C.

EXAMPLE 161

2-Furanyl(7-phenylpyrazolo[1,5-a]pyrimidin-3-yl)methanone

A mixture of 0.86 g of (3-amino-1H-pyrazol-4-yl)-2-furanylmethanone and 0.63 g of 1-phenyl-1-propynone in 35 ml of ethanol was heated on a steam bath for one hour, then chilled in an ice bath. The solid was collected giving 0.43 g of intermediate uncyclized product, mp 190°–194° C.

A 100 mg portion of this intermediate was heated in 20 ml of ethanol containing a catalytic amount of p-toluenesulfonic acid for 20 minutes on a steam bath. The solvent was removed and the residue partitioned between dichloromethane and dilute sodium hydroxide. The organic layer was heated and concentrated while adding hexane. When crystals began to form, the mixture was allowed to cool to room temperature. Filtration gave 75 mg of the desired product as off-white crystals having a melting point of 185°–187° C. and a pmr spectrum identical to that of the product prepared as described in Example 22.

EXAMPLE 162

2-Furanyl(7-phenylpyrazolo[1,5-a]pyrimidin-3-yl)methanone

A mixture of 0.86 g of (3-amino-1H-pyrazol-4-yl)-2-furanylmethanone and 0.63 g of 1-phenyl-1-propynone in 25 ml of ethanol with a catalytic amount of p-toluenesulfonic acid was heated on a steam bath for 1.5 hours. The mixture was chilled and then filtered giving 1.0 g of yellow solid. This solid was dissolved in a small amount of dichloromethane and placed on a silica gel column. The column was eluted with ethyl acetate:hexane (1:20) with a gradual change to ethyl acetate:hexane (2:5) as eluent. The column was then washed with ethyl acetate and the ethyl acetate wash was concentrated to a solid. This solid was cyrstallized from dichloromethane, giving 0.85 g of the desired product as cream crystals having a melting point of 188°–190° C. and a pmr spectrum identical to that of the product prepared as described in Example 22.

EXAMPLE 163

2-Furanyl(7-phenylpyrazolo[1,5-a]pyrimidin-3-yl)methanone

A mixture of 0.86 g of (3-amino-1H-pyrazol-4-yl)-2-furanylmethanone and 0.63 g of 1-phenyl-1-propynone in 35 ml of ethanol with several drops of boron trifluoride etherate was refluxed for 18 hours. The solvent was removed and the residue chromatographed on silica gel with ethyl acetate:hexane (1:20) as eluent and a gradual change to ethyl acetate:hexane (2:5). Elution with ethyl acetate gave a solid which was recrystallized from dichloromethanehexane, giving the desired product, mp 185°–187° C.

EXAMPLE 164

Phenyl[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone, pyridine-1-oxide

A 1.5 g portion of phenyl[7-(3-pyridinyl)-pyrazolo[1,5-a]pyrimidin-3-yl]methanone in 200 ml of dichloromethane was reacted as described in Example 132, giving 1.05 g of the desired product, mp 265°–267° C.

EXAMPLE 165

(4-Methoxyphenyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone, pyridine-1-oxide

A 1.65 g portion of (4-methoxyphenyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone in 200 ml of dichloromethane was reacted as described in Example 132, giving 0.37 g of the desired product, mp 254°–257° C.

EXAMPLE 166

[7-[3-(Ethylamino)phenyl]pyrazolo[1,5-a]pyrimidin-3-yl]-2-furanylmethanone

N-(3-Acetylphenyl)-4-methylbenzenesulfonamide was prepared by the method of R. H. Vloth, et al., J. Med. Chem., 9, 88 (1966).

A 29 g portion of N-(3-acetylphenyl)-4-methylbenzenesulfonamide was dissolved in 250 ml of dimethylformamide with stirring. This mixture was treated with 6.5 g of sodium methoxide and stirred for 30 minutes, then 20 g of ethyl iodide was added. This mixture was stirred at room temperature for one hour, then at reflux for 5 hours. The dimethylformamide was removed in vacuo, the residue shaken with 150 ml of water, the mixture adjusted to pH 4 with 10N sodium hydroxide and then cooled to 0° C. The precipitate was collected, washed twice with water and then air dried, giving 31.5 g of N-(3-acetylphenyl)-N-ethyl-4-methylbenzenesulfonamide.

A 31.2 g portion of N-(3-acetylphenyl)-N-ethyl-4-methylbenzenesulfonamide and 50 ml of dimethylformamide dimethylacetal were combined and stirred on a steam bath for 18 hours, then evaporated in vacuo to an oil. This oil was triturated with hexane at −10° C. The hexane was decanted and the residue dissolved in 125 ml of boiling dichloromethane and then filtered. The filtrate was reheated to boiling, 200 ml of hexane was added and the mixture cooled to −10° C. The precipitate was collected, washed with hexane and dried, giving 21.6 g of N-[3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]-N-ethyl-4-methylbenzenesulfonamide.

A mixture of 5.9 g of (3-amino-1H-pyrazol-4-yl)-2-furanylmethanone, 12.4 g of N-[3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]-N-ethyl-4-methylbenzenesulfonamide and 200 ml of glacial acetic acid was refluxed for 18 hours, then cooled to room temperature and evaporated to dryness. The residue was partitioned between 200 ml of dichloromethane and 100 ml of saturated aqueous sodium bicarbonate. The dichloromethane layer was dried, then filtered through hydrous magnesium silicate and washed with 200 ml of dichloromethane. The filtrate and wash were combined with 200 ml of hexane, concentrated to 250 ml, diluted with 100 ml of hexane and concentrated to turbidity. A heavy oil formed which was separated and cooled to −10° C. producing a solid. This solid was washed with hexane and then dried in vacuo at 60° C. giving N-ethyl-N-[3-[3-(2-furanylcarbonyl)pyrazolo[1,5-a]pyrimidin-7-yl]phenyl]-4-methylbenzenesulfonamide.

A 10.7 g portion of N-ethyl-N-[3-[3-(2-furanylcarbonyl)pyrazolo[1,5-a]pyrimidin-7-yl]phenyl]-4-methylbenzenesulfonamide was added to a mixture of 90 ml of water and 210 ml of concentrated sulfuric acid. This mixture was heated to 140°–145° C., allowed to cool slowly to room temperature, then cooled to −10° C., poured onto ice, made basic with 550 ml of concentrated ammonium hydroxide and cooled to 0° C. This mixture was extracted with dichloromethane. The extract was passed through hydrous magnesium silicate and washed with 200 ml of dichloromethane. The dichloromethane filtrate and wash was combined with 300 ml of hexane, concentrated to 300 ml, diluted to 800 ml with hexane, treated with charcoal, clarified and cooled to −10° C. This material was filtered, the filtrate concentrated to turbidity and cooled at −10° C. The precipitate was collected, washed with hexane and dried at 60° C. in vacuo, giving 2.3 g of the desired product, mp 142°–143° C.

EXAMPLE 167

[7-[3-(Ethylamino)phenyl]pyrazolo[1,5-a]pyrimidin-3-yl]phenylmethanone

A mixture of 6.2 g of 3-amino-1H-pyrazol-4-yl)-2-phenylmethanone and 12.4 g of N-[3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]-N-ethyl-4-methylbenzenesulfonamide was reacted as described in Example 166, giving 1.4 g of the desired product, mp 98°–99° C.

EXAMPLE 168

N-[3-[3-(Dimethylamino)-1-oxo-2-propenyl]phenyl-]acetamide

A 30.0 g portion of 3-acetamidoacetophenone was heated with 50 ml of dimethylformamide dimethylacetal on a steam bath under inert atmosphere for 8 hours. After cooling, the precipitated material was collected by filtration to yield the desired material as orange crystals (37.20 g, mp 184°–185° C.).

EXAMPLE 169

N-[3-[3-(Dimethylamino)-1-oxo-2-propenyl]phenyl]-propanamide

In the manner of the above example, substituting 3-propanamidoacetophenone for 3-acetamidoacetophenone gave the desired product as pale orange crystals, mp 106°–108° C.

EXAMPLE 170

N-[3-[3-Dimethylamino)-1-oxo-2-propenyl]phenyl]-butanamide

In the manner of Example 168, substituting 3-butanamidoacetophenone for 3-acetamidoacetophenone gave the desired compound as yellow-orange crystals, mp 113°–115° C.

EXAMPLE 171

N-[4-[3-(Dimethylamino)-1-oxo-2-propenyl]phenyl-]acetamide

In the manner of Example 168, substituting 4-acetamidoacetophenone for 3-acetamidoacetophenone gave the desired compound as pale yellow crystals, mp 185°–186° C.

EXAMPLE 172

N-[4-[3-(Dimethylamino)-1-oxo-2-propenyl]phenyl]-propanamide

In the manner of Example 168, substituting 4-propanamidoacetophenone for 3-acetamidoacetophenone gave the desired compound as yellow-orange crystals, mp 161°–163° C.

EXAMPLE 173

N-[3-[3-(Dimethylamino)-1-oxo-2-propenyl]phenyl]-N-methylacetamide

A solution of 4.62 g of N-[3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]acetamide in 25 ml of dimethylformamide was stirred in an inert atmosphere and 1.0 g of sodium hydride (60% oil suspension) was added. After stirring for 1 hour, the liberation of hydrogen had ceased and a solution of 3.0 g of methyl iodide in 10 ml

of dimethylformamide was gradually added (with cooling, if necessary). After stirring for an additional 1 hour at room temperature, any volatiles were removed at reduced pressure and then the reaction mixture was triturated 3 times with 100 ml of hexane. The reaction mixture was carefully poured into cold water and extracted exhaustively with methylene chloride. This material was evaporated at reduced pressure to yield a yellow-orange solid. A solution of the crude solid in methylene chloride was passed through a pad of hydrous magnesium silicate. Addition of hexane to the refluxing eluate gave crystals which were collected after cooling. The desired compound was a yellow-orange crystalline material, mp 146°–148° C.

EXAMPLE 174

N-[3-[3-(Dimethylamino)-1-oxo-2-propenyl]phenyl]-N-ethylacetamide

In the manner of Example 173 substituting ethyl iodide for methyl iodide and following the procedure outlined above, the desired compound was isolated as yellow-orange crystals, mp 110°–113° C.

EXAMPLE 175

N-[3-[3-(Dimethylamino)-1-oxo-2-propenyl]phenyl]-N-methylpropanamide

In the manner of Example 173, substituting N-[3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]propanamide for N-[3-[3-(dimethylamino)-1-oxo-2-propenyl]-phenyl]acetamide and following the procedure outlined in Example 173, the desired product was isolated as a pale yellow crystalline solid, mp 148°–149° C.

EXAMPLE 176

N-[3-[3-(Dimethylamino)-1-oxo-2-propenyl]phenyl]-N-ethylpropanamide

In the manner of Example 175, substituting ethyl iodide for methyl iodide and following the exact procedure in Example 173, the desired material was isolated as a yellow crystalline solid, mp 105°–107° C.

EXAMPLE 177

N-[4-[3-(Dimethylamino)-1-oxo-2-propenyl]phenyl]-N-methylpropanamide

A soluton of 3.10 g of N-[4-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]propanamide in 25 ml dimethylformamide was stirred in an inert atmosphere and 0.60 g of sodium hydride (60% oil suspension) was added. After stirring for 1 hour, the liberation of hydrogen had ceased and a solution of 1.8 g of methyl iodide in 5 ml of dimethylformamide was added portionwise. After stirring for an additional hour, the system was evaporated to remove volatiles and then the reaction mixture was triturated 3 times with hexane (3×50 ml). The reaction mixture was carefully poured into cold water and extracted with methylene chloride. The methylene chloride solution was dried and evaporated to dryness at reduced pressure to yield a crystalline solid. Recrystallization from methylene chloridehexane gave a yellow crystalline solid, mp 76°–78° C.

EXAMPLE 178

N-[4-[3-(Dimethylamino)-1-oxo-2-propenyl]phenyl]-N-ethylpropanamide

In the manner of Example 177, substituting ethyl iodide for methyl iodide and following the procedure outlined in that example, the desired compound was isolated as a low melting yellow-orange crystalline compound, mp 75°–77° C.

EXAMPLE 179

N-[3-(3-Benzylpyrazolo[1,5-a]pyrimidin-7-yl)phenyl-]acetamide

A solution of 1.87 g of 3-amino-4-benzoylpyrazole and 2.32 g of N-[3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]acetamide (Example 168) in 50 ml of glacial acetic acid was refluxed for 8 hours. The reaction mixture was evaporated to dryness and a saturated sodium bicarbonate solution was added along with 400 ml of methylene chloride. The solid that separated was recovered by filtration and was the desired compound (2.57 g, mp 205°–207° C.). The methylene chloride solution afforded more compound (0.73 g, mp 205°–207° C.).

EXAMPLE 180

N-[3-(3-Benzoylpyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N-methylacetamide

In the manner of Example 179, substituting N-[3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]-N-methylacetamide (Example 171) for N-[3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]acetamide gave the desired product, mp 162°–164° C.

EXAMPLE 181

N-[3-(3-Benzoylpyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N-ethylacetamide

In the manner of Example 179, substituting N-[3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]-N-ethylacetamide (Example 174) for N-[3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]acetamide gave the product of the example, mp 158°–160° C.

EXAMPLE 182

N-[3-[3-(2-Furancarbonyl)pyrazolo[1,5-a]pyrimidin-7-yl]phenyl]acetamide

A solution of 1.77 g of 3-amino-4-furanylpyrazole and 2.32 g of N-[3-[3-(dimethylamino)-1-oxo-2-propenyl]-phenyl]acetamide (Example 168) in 50 ml of glacial acetic acid was refluxed for 10 hours. Evaporation of the reaction mixture gave a solid which was treated with a saturated sodium bicarbonate solution and 200 ml of methylene chloride. The solid that precipitated was recovered by filtration and proved to be the desired product (2.57 g, mp 195°–196° C.). An additional quantity of product was isolated from the methylene chloride solution, mp 195°–196° C.

EXAMPLE 183

N-[3-[3-(2-Furancarbonyl)pyrazolo[1,5-a]pyrimidin-7-yl]phenyl]-N-methylacetamide

In the manner of the above example, substituting N-[3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]-N-methylacetamide (Example 171) for N-[3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]acetamide gave the desired product, mp 210°–212° C., which was isolated from the methylene chloride solution.

EXAMPLE 184

N-Ethyl-N-[3-[3-(2-furanylcarbonyl)pyrazolo[1,5-a]pyrimidin-7-yl]acetamide

In the manner of Example 182, substituting N-[3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]-N-ethylacetamide (Example 174) for N-[3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]acetamide gave the desired product isolated from the methylene chloride extract, mp 194°–196° C.

EXAMPLE 185

N-[3-(3-Benzoylpyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-propanamide

A solution of 1.87 g of 3-amino-4-benzoylpyrazole and 2.46 g of N-[3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]propanamide (Example 169) in 50 ml of glacial acetic acid was refluxed for 15 hours and then evaporated to yield a pale yellow gum. This material was partitioned between an aqueous saturated sodium bicarbonate solution and methylene chloride. The methylene chloride solution was dried with powdered anhydrous sodium sulfate and then passed through a short column of hydrous magnesium silicate adsorbent. The eluate was refluxed in a steam bath and hexane gradually added until turbidity. After cooling, the desired product was recovered by filtration (2.39 g, mp 172°–174° C.).

EXAMPLE 186

N-[3-(3-Benzoylpyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-N-methylpropanamide

In the manner of the above example substituting N-[3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]-N-methylpropanamide (Example 175) for N-[3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]propanamide gave the desired compound, mp 154°–156° C.

EXAMPLE 187

N-[3-(3-Benzoylpyrazolo[1,5-a]pyrimidin-7-yl)phenyl]N-ethylpropanamide

In the manner of Example 185, substituting N-[3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]-N-ethyl-propanamide for N-[3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]propanamide gave the desired compound, mp 194°–195° C.

EXAMPLE 188

N-[3-[3-(2-Furanylcarbonyl)pyrazolo[1,5-a]pyrimidin-7-yl]phenyl]propanamide

A solution of 1.77 g 3-amino-4-furanylpyrazole and 2.46 g of N-[3-[3-(dimethylamino)-1-oxo-2-propenyl]-phenyl]propanamide in 50 ml of glacial acetic acid was refluxed for 8 hours. Removal of all solvents gave a gum which was partitioned between an aqueous saturated sodium bicarbonate solution and methylene chloride. The methylene chloride extract was dried with powdered anhydrous sodium sulfate and then passed through a short column of a hydrous magnesium silicate adsorbent. The eluate was refluxed on a steam bath with gradual addition of hexanes until turbidity was noted. The desired product was collected by filtration of the cooled crystallization mixture, (2.05 g, mp 185°–186° C.).

EXAMPLE 189

N-[3-[3-(2-Furanylcarbonyl)pyrazolo[1,5-a]pyrimidin-7-yl]phenyl]-N-methylpropanamide

In the manner of the above example, substituting N-[3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]-N-methylpropanamide for N-[3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]propanamide gave the desired product, mp 153°–155° C.

EXAMPLE 190

N-Ethyl-N-[3-[3-(2-furanylcarbonyl)pyrazolo[1,5-a]pyrimidin-7-yl]phenyl]propanamide

In the manner of Example 188, substituting N-[3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]-N-ethyl-propanamide (Example 176) for N-[3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]propanamide gave the desired compound, mp 165°–167° C.

EXAMPLE 191

N-[4-(3-Benzoylpyrazolo[1,5-a]pyrimidin-7-yl)phenyl]acetamide

In the manner of Example 179, substituting N-[4-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]acetamide for N-[3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]acetamide gave the desired compound, mp 229°–231° C.

EXAMPLE 192

N-[4-(3-Benzoylpyrazole[1,5-a]pyrimidin-7-yl)phenyl]-N-methylacetamide

In the manner of Example 179, substituting N-[4-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]-N-methylacetamide for N-[3-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]acetamide gave the desired product, mp 173°–175° C.

EXAMPLE 193

N-[4-[3-(2-Furanylcarbonyl)pyrazolo[1,5-a]pyrimidin-7-yl]phenyl]-N-methylacetamide

A solution of 1.77 g of 3-amino-4-furanylpyrazole and 2.46 g of N-[4-[3-(dimethylamino)-1-oxo-2-propenyl]-phenyl]-N-methylacetamide in 50 ml of glacial acetic acid was refluxed for 8 hours. Evaporation of the reaction mixture gave a gum which was partitioned between an aqueous saturated sodium bicarbonate solution and methylene chloride. The methylene chloride extract was dried and passed through a short column of hydrous magnesium silicate adsorbent. The eluate was refluxed on a steam bath with gradual addition of hexane until turbidity. On cooling, the desired compound was collected by filtration, mp 202°–204° C.

EXAMPLE 194

N-[4-(3-Benzoylpyrazolo[1,5-a]pyrimidin-7-yl)phenyl]-propanamide

In the manner of Example 179, substituting N-[4-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]propanamide for N-[3-[3-(dimethylamino)-1-oxo-2-propenyl]-phenyl]acetamide gave the desired product, mp 211°–213° C.

EXAMPLE 195

N-[4-[3-(2-Furanylcarbonyl)pyrazolo[1,5-a]pyrimidin-7-yl]phenyl]propanamide

In the manner of Example 188, substituting N-[4-[3-(dimethylamino)-1-oxo-2-propenyl]phenyl]propanamide for N-[3-[3-(dimethylamino)-1-oxo-2-propenyl]-phenyl]propanamide gave the desired product, mp 235°–237° C.

EXAMPLE 196

[5-Methyl-7-(2-thienyl)pyrazolo[1,5-a]pyrimidin-3-yl]phenyl-methanone

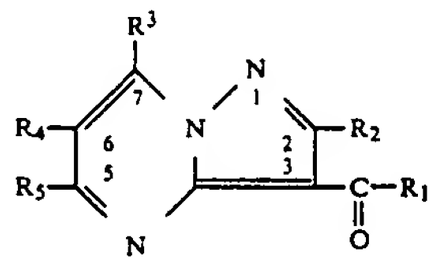
A mixture of 0.01 mole of 1-(2-thienyl)butan-1,3-dione was reacted with pyrrolidine in ethyl acetate to give 3-(1-pyrrolidinyl)-1-(2-thienyl)-2-buten-1-one, mp 154°–156° C.

The title compound may then be prepared as follows:

A 0.10 mole portion of the above compound and 0.10 mole of (3-amino-1H-pyrazol-4-yl)phenyl-methanone in 75 ml of glacial acetic acid is refluxed for 6 hours. The solvent is removed and the product isolated as described in Example 1.

We claim:

1. A compound selected from those of the formula:



wherein R_1 is selected from the group consisting of unsubstituted phenyl; phenyl mono- or di-substituted by halogen, alkoxy(C_1–C_3) or alkyl(C_1–C_3); phenyl mono-substituted by trifluoromethyl, alkylthio(C_1–C_3), alkylamino(C_1–C_3), dialkylamino(C_1–C_3), methylenedioxy, alkylsulfonyl(C_1–C_3) or alkanoylamino(C_1–C_3); naphthalenyl; thiazolyl; biphenyl; thienyl; furanyl; pyridinyl; substituted thiazolyl; substituted biphenyl; substituted thienyl; and substituted pyridinyl wherein the substituents are selected from one or two of the group consisting of halogen, alkoxy(C_1–C_3) and alkyl(C_1–C_3); R_2, R_4 and R_5 are each selected from the group consisting of hydrogen and alkyl(C_1–C_3); and R_3 is selected from the group consisting of unsubstituted phenyl, phenyl mono-substituted by halogen, trifluoromethyl, alkoxy(C_1–C_3), amino, alkyl(C_1–C_3), alkylamino(C_1–C_6), dialkylamino(C_1–C_3), alkanoylamino(C_1–C_6), N-alkyl(C_1–C_6)alkanoylamino(C_1–C_6), cyano or alkylthio(C_1–C_3); furanyl; thienyl; pyridinyl; and pyridine-1-oxide.

2. A compound according to claim 1, wherein R_1 is 2-furanyl; R_2, R_4 and R_5 are each hydrogen; and R_3 is selected from the group consisting of 3-(trifluoromethyl)phenyl; 3-pyridinyl; and 4-pyridinyl.

3. A compound according to claim 1, wherein R_1 is selected from the group consisting of unsubstituted phenyl; phenyl substituted by 4-methyl, 4-ethyl, 4-methoxy, 3,4-dimethoxy or 4-dimethylamino; 2-furanyl; 2-thienyl; 2-pyridinyl; and 4-pyridinyl; R_2, R_4 and R_5 are each hydrogen; and R_3 is selected from the group consisting of 3-(trifluoromethyl)phenyl; 3-pyridinyl; 4-pyridinyl; 3-[N-alkyl(C_1–C_6)alkanoylamino(C_1–C_6)]-phenyl; and 3-[alkylamino(C_1–C_6)].

4. The compound according to claim 1, phenyl[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone.

5. The compound according to claim 1, (4-fluorophenyl)[7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]-methanone.

6. The compound according to claim 1, phenyl[7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone.

7. The compound according to claim 1, phenyl[7-[3-(trifluoromethyl)phenyl]pyrazolo[1,5-a]pyrimidin-3-yl]methanone.

8. The compound according to claim 1, (4-methoxyphenyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone.

9. The compound according to claim 1, (3-fluorophenyl)[7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone.

10. The compound according to claim 1, [7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl][3-(trifluoromethyl)phenyl]methanone.

11. The compound according to claim 1, 2-thienyl[7-[3-(trifluoromethyl)phenyl]pyrazolo[1,5-a]pyrimidin-3-yl]methanone.

12. The compound according to claim 1, 2-furanyl[7-[3-(trifluoromethyl)phenyl]pyrazolo[1,5-a]pyrimidin-3-yl]methanone.

13. The compound according to claim 1, 2-furanyl[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone.

14. The compound according to claim 1, [2-methyl-7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]phenylmethanone.

15. The compound according to claim 1, (4-methylphenyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone.

16. The compound according to claim 1, phenyl[7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone, pyridine-1-oxide.

17. The compound according to claim 1, 2-pyridinyl[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone.

18. The compound according to claim 1, 2-pyridinyl[7-[3-(trifluoromethyl)phenyl]pyrazolo[1,5-a]pyrimidin-3-yl]methanone.

19. The compound according to claim 1, 2-pyridinyl[7-(4-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone.

20. The compound according to claim 1, [7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]-2-thiazolyl-methanone.

21. The compound according to claim 1, 4-pyridinyl[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone.

22. The compound according to claim 1, 4-pyridinyl[7-[3-(trifluoromethyl)phenyl]pyrazolo[1,5-a]pyrimidin-3-yl]methanone.

23. The compound according to claim 1, (2-fluorophenyl)[7-(3-pyridinyl)pyrazolo[1,5-a]pyrimidin-3-yl]methanone.

24. The compound according to claim 1, (2-fluorophenyl)[7-[3-(trifluoromethyl)phenyl]pyrazolo[1,5-a]pyrimidin-3-yl]methanone.

25. The compound according to claim 1, [7-[3-(ethylamino)phenyl]pyrazolo[1,5-a]pyrimidin-3-yl]-2-furanylmethanone.

26. The compound according to claim 1, [7-[3-(ethylamino)phenyl]pyrazolo[1,5-a]pyrimidin-3-yl]phenylmethanone.

27. A method of meliorating anxiety in a mammal suffering from anxiety which comprises administering to said mammal an effective anxiolytic amount of a compound of claim 1.

28. A method of treating epilepsy in a mammal suffering from epilepsy which comprises administering to said mammal an effective anticonvulsant amount of a compound of claim 1.

29. A method of inducing sedation or hypnosis in a mammal which comprises administering to said mammal an effective sedative or hypnotic amount of a compound of claim 1.

30. A method of inducing skeletal muscle relaxation in a mammal which comprises administering to said mammal an effective skeletal muscle relaxant amount of a compound of claim 1.

31. A composition of matter in dosage unit form comprising from 2-750 mg of a compound of claim 1 in association with a pharmaceutically acceptable carrier.

* * * * *

EXHIBIT D

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office

Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

SERIAL NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
06/732,986	05/13/85	DUSZA J	29,955

SUSAN H. RAUCH
1937 W. MAIN ST., P.O. BOX 60
STAMFORD, CT 06904-0060

EXAMINER	
KAPNER, S	
ART UNIT	PAPER NUMBER
122	2

DATE MAILED: 11/22/85

This is a communication from the examiner in charge of your application.

COMMISSIONER OF PATENTS AND TRADEMARKS

Feb. 22, 1986

☑ This application has been examined ☐ Responsive to communication filed on _____ ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), _____ days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☑ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449
4. ☐ Notice of Informal Patent Application, Form PTO-152
5. ☐ Information on How to Effect Drawing Changes, PTO-1474
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☑ Claims 1-19 are pending in the application.

   Of the above, claims 15-17 and 19 are withdrawn from consideration.

2. ☐ Claims _____ have been cancelled.

3. ☐ Claims _____ are allowed.

4. ☑ Claims 1-14 and 18 are rejected.

5. ☐ Claims _____ are objected to.

6. ☐ Claims _____ are subject to restriction or election requirement.

7. ☐ This application has been filed with informal drawings which are acceptable for examination purposes until such time as allowable subject matter is indicated.

8. ☐ Allowable subject matter having been indicated, formal drawings are required in response to this Office action.

9. ☐ The corrected or substitute drawings have been received on _____. These drawings are ☐ acceptable; ☐ not acceptable (see explanation).

10. ☐ The ☐ proposed drawing correction and/or the ☐ proposed additional or substitute sheet(s) of drawings, filed on _____, has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).

11. ☐ The proposed drawing correction, filed _____, has been ☐ approved. ☐ disapproved (see explanation). However, the Patent and Trademark Office no longer makes drawing changes. It is now applicant's responsibility to ensure that the drawings are corrected. Corrections MUST be effected in accordance with the instructions set forth on the attached letter "INFORMATION ON HOW TO EFFECT DRAWING CHANGES", PTO-1474.

12. ☐ Acknowledgment is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.

13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

14. ☐ Other

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-18, drawn to compounds, compositions and a method of use, classified in Class 544, subclass 281 and Class 514, subclass 258.

II. Claim 19, drawn to a process for making the compounds, classified in Class 544, subclass 281.

In the event that the invention of group I is elected, a single method of use must be chosen.

The inventions are distinct, each from the other, because of the following reasons:

Inventions I and II are related as process of making and product made.

The inventions are distinct if either (1) the process as claimed can be used to make another and materially different product, or (2) the product as claimed can be made by another and materially different process. MPEP 806.05(f).

In this case, the product as claimed can be made by a materially different process such as that described in Dugza '422.

The inventions of group I, claims 14-17 are distinct because the product may be used in four materially different processes as set forth in claims 14-17. See MPEP 806.05(h).

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject

matter, restriction for examination purposes as indicated is proper.

During a telephone conversation with Susan H. Rauch on November 6, 1985 a provisional election was made with right of traverse to prosecute the invention of group I, claims 1-14 and 18. Affirmation of this election must be made by applicant in responding to this Office action. Claims 15-17 and 19 are withdrawn from further consideration by the examiner as being drawn to a nonelected invention. See 37 CFR 1.142(b).

The method of use of claim 14 was elected.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(h).

Claims 1-14 and 18 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the prior invention as set forth in claims 1-31 of U.S. patent no. 4,521,422. Although the conflicting claims are not identical, they are not patentably distinct from each other because the distinction between the R_4 substituents claimed instantly and the R_1 groups of '422 is not deemed patentable.

KCM. 11/30/85.

Claims 1-14 and 18 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-14 and 18 of copending application serial no. 732,985. Although the conflicting claims are not identical, they are not patentably distinct from each other because the differences in substituents between R_1 in 732,985 and R_4 instantly are not deemed patentably distinct.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The obviousness-type double patenting rejection is a judicially established doctrine based upon public policy and is primarily intended to prevent prolongation of monopoly by prohibiting claims in a second patent not patentably distinct from claims in a first patent. In re Vogel, 164 USPQ 619 (CCPA 1970). A timely filed terminal disclaimer in compliance with 37 CFR 1.321(b) would overcome an actual or provisional rejection on this ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78(d).

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Copies of references are not provided since they are applicants own and are therefore presumed to be easily obtainable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to S. Kapner whose telephone number is (703) 557-3979.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 557-3920.

SK
Kapner:ce
11-13-85

Mark L. Berch
Primary Examiner
Art Unit 122

KCM 12/30/85

EXHIBIT E

29,995

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

JOHN PAUL DUSZA,
ANDREW STEPHEN TONCUFCIK and
JAY DONALD ALBRIGHT

Serial No.: 732,986 Group Art Unit: 122

Filed: May 13, 1985 Examiner: S. Kapner

For: [7-(3-DISUBSTITUTED AMINO)-PHENYL]PYRAZOLO[1,5-a]-PYRIMIDINES

Commissioner of Patents
and Trademarks
Washington, D.C. 20231

S I R :

TERMINAL DISCLAIMER PURSUANT
TO 37 C.F.R. 1.321(b)

Your petitioner, AMERICAN CYANAMID COMPANY, a corporation organized and existing under the laws of the State of Maine and having its executive offices at One Cyanamid Plaza, Wayne, in the County of Passaic and State of New Jersey, represents that it is the assignee of the entire right, title and interest in application Serial No. 732,986, filed May 13, 1985, for [7-(3-DISUBSTITUTED AMINO)PHENYL]PYRAZOLO[1,5-a]PYRIMIDINES by an assignment recorded in the United States Patent and Trademark Office on May 13, 1985.

Your petitioner, AMERICAN CYANAMID COMPANY, hereby disclaims the terminal part of any patent granted on the above-identified application which would extend beyond June 3, 2002, and hereby agrees that any patent so granted on the above-identified application shall be enforceable only for and during such period that the legal title to said patent shall be the same as the legal title to United States Letters Patent No. 4,521,422 and to any patent which might issue on application Serial No. 732,985; this agreement to run with any patent granted on the above-identified application and to be binding upon the grantee, its successors or assigns.

AMERICAN CYANAMID COMPANY

By John T. Hagan
John T. Hagan, Manager
Patent Law Department

EXHIBIT F

29,995

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

JOHN PAUL DUSZA,
ANDREW STEPHEN TOMCUFCIK and
JAY DONALD ALBRIGHT

Serial No.: 732,986 Group Art Unit: 122

Filed: May 13, 1985 Examiner: S. Kapner

For: [7-(3-DISUBSTITUTED AMINO)-PHENYL]PYRAZOLO[1,5-a]-PYRIMIDINES

Stamford, Connecticut
April 21, 1986

Commissioner of Patents
and Trademarks
Washington, D.C. 20231

Sir:

AMENDMENT

In response to the Office Action mailed November 22, 1985, kindly amend the above-identified case as follows:

IN THE SPECIFICATION:

Page 1, line 3 (of CROSS REFERENCE), after "May 24, 1984," insert -- Patent No. 4,521,422, --.

Page 4, line 16, delete "of our copending application Serial No." and substitute therefor -- U.S. Patent No. 4,521,422, --; and

line 17, delete "612,812,".

IN THE CLAIMS:

Cancel Claims 15-17 and 19.

REMARKS

Applicants affirm their election to prosecute the invention of Group I, i.e., Claims 1-14 and 18. Moreover, Applicants cancel Claims 15-17 and 19. Notwithstanding cancelation of Claims 15-17 and 19, the inventorship of the Application is unchanged. Each of the originally-designated Applicants remains an inventor of the Application as amended.

Applicants have amended the Specification on pages 1 and 4 to reflect the issuance of their co-pending Application Serial No. 612,812 as U.S. Patent No. 4,521,422. These amendments do not constitute new matter.

Claims 1-14 and 18 are rejected as double patenting of the obviousness type over U.S. Patent No. 4,521,422 and provisionally rejected as double patenting of the obviousness type over their

copending Application Serial No. 732,985. To overcome these rejections, pursuant to 37 C.F.R. §1.321(b), Applicants are submitting herewith Assignee's disclaimer of the term of any patent granted on the above-identified Application which would extend beyond the expiration date of U.S. Patent No. 4,521,422 (June 3, 2002) and Assignee's acknowledgement that any patent granted on said Application would be enforceable only for such time as its legal title is identical to the legal title of U.S. Patent No. 4,521,422 and to any patent which might issue on Application Serial No. 732,985.

In view of the terminal disclaimer, Claims 1-14 and 18 are patentable over U.S. Patent No. 4,521,422 and any patent issuing on Application Serial No. 732,985.

Applicants' attorney has reviewed the references cited but not applied by the Examiner, and agrees that the instant invention is patentable thereover.

This Application now being in condition for allowance, Applicants request that the Examiner allow it to issue.

Authorization for the fee for an extension of time to reply pursuant to 37 C.F.R. §§1.136 and 1.17 to be charged to Assignee's Deposit Account is contained in the Petition submitted herewith. No additional fees are due.

Respectfully submitted,

Susan H. Rauch

Susan H. Rauch
Attorney of Record
Registration No. 31,130

AMERICAN CYANAMID COMPANY
1937 West Main Street
Stamford, Connecticut
06904-0060
(203)348-7331 ext. 2701

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner of Patents and Trademarks, Washington, D. C. 20231, on April 21, 1992
(Date of Deposit)

Susan H. Rauch
Name of Applicant, Assignee, or Registered Representative

Susan H. Rauch
Signature

April 21, 1992
Date of Signature

EXHIBIT G

"(A) while domiciled in the United States, and serving in any other country in connection with operations by or on behalf of the United States,

"(B) while domiciled in a NAFTA country and serving in another country in connection with operations by or on behalf of that NAFTA country, or

"(C) while domiciled in a WTO member country and serving in another country in connection with operations by or on behalf of that WTO member country,

that person shall be entitled to the same rights of priority in the United States with respect to such invention as if such invention had been made in the United States, that NAFTA country, or that WTO member country, as the case may be.

"(3) USE OF INFORMATION.—To the extent that any information in a NAFTA country or a WTO member country concerning knowledge, use, or other activity relevant to proving or disproving a date of invention has not been made available for use in a proceeding in the Patent and Trademark Office, a court, or any other competent authority to the same extent as such information could be made available in the United States, the Commissioner, court, or such other authority shall draw appropriate inferences, or take other action permitted by statute, rule, or regulation, in favor of the party that requested the information in the proceeding.

"(b) DEFINITIONS.—As used in this section—

"(1) the term 'NAFTA country' has the meaning given that term in section 2(4) of the North American Free Trade Agreement Implementation Act; and

"(2) the term 'WTO member country' has the meaning given that term in section 2(10) of the Uruguay Round Agreements Act.".

(b) EFFECTIVE DATE.— 35 USC 104 note.

(1) IN GENERAL.—Except as provided in paragraph (2), the amendment made by this section shall apply to all patent applications that are filed on or after the date that is 12 months after the date of entry into force of the WTO Agreement with respect to the United States.

(2) ESTABLISHMENT OF DATE.—An applicant for a patent, or a patentee, may not establish a date of invention for purposes of title 35, United States Code, that is earlier than 12 months after the date of entry into force of the WTO Agreement with respect to the United States by reference to knowledge or use, or other activity, in a WTO member country, except as provided in sections 119 and 365 of such title.

SEC. 532. PATENT TERM AND INTERNAL PRIORITY.

(a) PATENT RIGHTS.—

(1) CONTENTS AND TERM OF PATENT.—Section 154 of title 35, United States Code, is amended to read as follows:

"§ 154. Contents and term of patent

"(a) IN GENERAL.—

"(1) CONTENTS.—Every patent shall contain a short title of the invention and a grant to the patentee, his heirs or assigns, of the right to exclude others from making, using, offering for sale, or selling the invention throughout the United States or importing the invention into the United States, and,

if the invention is a process, of the right to exclude others from using, offering for sale or selling throughout the United States, or importing into the United States, products made by that process, referring to the specification for the particulars thereof.

"(2) TERM.—Subject to the payment of fees under this title, such grant shall be for a term beginning on the date on which the patent issues and ending 20 years from the date on which the application for the patent was filed in the United States or, if the application contains a specific reference to an earlier filed application or applications under section 120, 121, or 365(c) of this title, from the date on which the earliest such application was filed.

"(3) PRIORITY.—Priority under section 119, 365(a), or 365(b) of this title shall not be taken into account in determining the term of a patent.

"(4) SPECIFICATION AND DRAWING.—A copy of the specification and drawing shall be annexed to the patent and be a part of such patent.

"(b) TERM EXTENSION.—

"(1) INTERFERENCE DELAY OR SECRECY ORDERS.—If the issue of an original patent is delayed due to a proceeding under section 135(a) of this title, or because the application for patent is placed under an order pursuant to section 181 of this title, the term of the patent shall be extended for the period of delay, but in no case more than 5 years.

"(2) EXTENSION FOR APPELLATE REVIEW.—If the issue of a patent is delayed due to appellate review by the Board of Patent Appeals and Interferences or by a Federal court and the patent is issued pursuant to a decision in the review reversing an adverse determination of patentability, the term of the patent shall be extended for a period of time but in no case more than 5 years. A patent shall not be eligible for extension under this paragraph if it is subject to a terminal disclaimer due to the issue of another patent claiming subject matter that is not patentably distinct from that under appellate review.

"(3) LIMITATIONS.—The period of extension referred to in paragraph (2)—

"(A) shall include any period beginning on the date on which an appeal is filed under section 134 or 141 of this title, or on which an action is commenced under section 145 of this title, and ending on the date of a final decision in favor of the applicant;

"(B) shall be reduced by any time attributable to appellate review before the expiration of 3 years from the filing date of the application for patent; and

"(C) shall be reduced for the period of time during which the applicant for patent did not act with due diligence, as determined by the Commissioner.

"(4) LENGTH OF EXTENSION.—The total duration of all extensions of a patent under this subsection shall not exceed 5 years.

"(c) CONTINUATION.—

"(1) DETERMINATION.—The term of a patent that is in force on or that results from an application filed before the date that is 6 months after the date of the enactment of the Uruguay

Round Agreements Act shall be the greater of the 20-year term as provided in subsection (a), or 17 years from grant, subject to any terminal disclaimers.

"(2) REMEDIES.—The remedies of sections 283, 284, and 285 of this title shall not apply to Acts which—

"(A) were commenced or for which substantial investment was made before the date that is 6 months after the date of the enactment of the Uruguay Round Agreements Act; and

"(B) became infringing by reason of paragraph (1).

"(3) REMUNERATION.—The acts referred to in paragraph (2) may be continued only upon the payment of an equitable remuneration to the patentee that is determined in an action brought under chapter 28 and chapter 29 (other than those provisions excluded by paragraph (2)) of this title.".

(2) PROVISION OF FURTHER LIMITED REEXAMINATION AND CONDITIONS OF RESTRICTION REQUIREMENTS.—(A) The Commissioner of Patents and Trademarks shall prescribe regulations to provide for further limited reexamination of applications that have been pending for 2 years or longer as of the effective date of section 154(a)(2) of title 35, United States Code, as added by paragraph (1) of this subsection, taking into account any reference made in such application to any earlier filed application under section 120, 121, or 365(c) of such title. The Commissioner may establish appropriate fees for such further limited reexamination.

35 USC 154 note.
Regulations.

(B) The Commissioner of Patents and Trademarks shall prescribe regulations to provide for the examination of more than 1 independent and distinct invention in an application that has been pending for 3 years or longer as of the effective date of section 154(a)(2) of title 35, United States Code, as added by paragraph (1) of this subsection, taking into account any reference made in such application to any earlier filed application under section 120, 121, or 365(c) of such title. The Commissioner may establish appropriate fees for such examination.

(b) ESTABLISHMENT OF A DOMESTIC PRIORITY SYSTEM.—

(1) IN GENERAL.—Section 119 of title 35, United States Code, is amended—

(A) by amending the section caption to read as follows:

"§ 119. Benefit of earlier filing date; right of priority";

(B) by designating the undesignated paragraphs as subsections (a), (b), (c), and (d), respectively; and

(C) by adding at the end the following:

"(e)(1) An application for patent filed under section 111(a) or section 363 of this title for an invention disclosed in the manner provided by the first paragraph of section 112 of this title in a provisional application filed under section 111(b) of this title, by an inventor or inventors named in the provisional application, shall have the same effect, as to such invention, as though filed on the date of the provisional application filed under section 111(b) of this title, if the application for patent filed under section 111(a) or section 363 of this title is filed not later than 12 months after the date on which the provisional application was filed and if it contains or is amended to contain a specific reference to the provisional application.

"(2) A provisional application filed under section 111(b) of this title may not be relied upon in any proceeding in the Patent and Trademark Office unless the fee set forth in subparagraph (A) or (C) of section 41(a)(1) of this title has been paid and the provisional application was pending on the filing date of the application for patent under section 111(a) or section 363 of this title.".

(2) FEES.—Section 41(a)(1) of title 35, United States Code, is amended by adding at the end the following:

"(C) On filing each provisional application for an original patent, $150.".

(3) APPLICATIONS.—Section 111 of title 35, United States Code, is amended to read as follows:

"§ 111. Application

"(a) IN GENERAL.—

"(1) WRITTEN APPLICATION.—An application for patent shall be made, or authorized to be made, by the inventor, except as otherwise provided in this title, in writing to the Commissioner.

"(2) CONTENTS.—Such application shall include—

"(A) a specification as prescribed by section 112 of this title;

"(B) a drawing as prescribed by section 113 of this title; and

"(C) an oath by the applicant as prescribed by section 115 of this title.

"(3) FEE AND OATH.—The application must be accompanied by the fee required by law. The fee and oath may be submitted after the specification and any required drawing are submitted, within such period and under such conditions, including the payment of a surcharge, as may be prescribed by the Commissioner.

"(4) FAILURE TO SUBMIT.—Upon failure to submit the fee and oath within such prescribed period, the application shall be regarded as abandoned, unless it is shown to the satisfaction of the Commissioner that the delay in submitting the fee and oath was unavoidable or unintentional. The filing date of an application shall be the date on which the specification and any required drawing are received in the Patent and Trademark Office.

"(b) PROVISIONAL APPLICATION.—

"(1) AUTHORIZATION.—A provisional application for patent shall be made or authorized to be made by the inventor, except as otherwise provided in this title, in writing to the Commissioner. Such application shall include—

"(A) a specification as prescribed by the first paragraph of section 112 of this title; and

"(B) a drawing as prescribed by section 113 of this title.

"(2) CLAIM.—A claim, as required by the second through fifth paragraphs of section 112, shall not be required in a provisional application.

"(3) FEE.—(A) The application must be accompanied by the fee required by law.

"(B) The fee may be submitted after the specification and any required drawing are submitted, within such period and

under such conditions, including the payment of a surcharge, as may be prescribed by the Commissioner.

"(C) Upon failure to submit the fee within such prescribed period, the application shall be regarded as abandoned, unless it is shown to the satisfaction of the Commissioner that the delay in submitting the fee was unavoidable or unintentional.

"(4) FILING DATE.—The filing date of a provisional application shall be the date on which the specification and any required drawing are received in the Patent and Trademark Office.

"(5) ABANDONMENT.—The provisional application shall be regarded as abandoned 12 months after the filing date of such application and shall not be subject to revival thereafter.

"(6) OTHER BASIS FOR PROVISIONAL APPLICATION.—Subject to all the conditions in this subsection and section 119(e) of this title, and as prescribed by the Commissioner, an application for patent filed under subsection (a) may be treated as a provisional application for patent.

"(7) NO RIGHT OF PRIORITY OR BENEFIT OF EARLIEST FILING DATE.—A provisional application shall not be entitled to the right of priority of any other application under section 119 or 365(a) of this title or to the benefit of an earlier filing date in the United States under section 120, 121, or 365(c) of this title.

"(8) APPLICABLE PROVISIONS.—The provisions of this title relating to applications for patent shall apply to provisional applications for patent, except as otherwise provided, and except that provisional applications for patent shall not be subject to sections 115, 131, 135, and 157 of this title.".

(c) CONFORMING CHANGES.—

(1) Section 156(a)(2) of title 35, United States Code, is amended by inserting "under subsection (e)(1) of this section" after "extended".

(2) Section 172 of title 35, United States Code, is amended—

(A) by striking "section 119" and inserting "subsections (a) through (d) of section 119"; and

(B) by inserting at the end the following new sentence: "The right of priority provided for by section 119(e) of this title shall not apply to designs.".

(3) Section 173 of title 35, United States Code, is amended by inserting "from the date of grant" after "years".

(4) Section 365 of title 35, United States Code, is amended—

(A) in subsection (a), by striking "section 119" and inserting "subsections (a) through (d) of section 119"; and

(B) in subsection (b), by striking "the first paragraph of section 119" and inserting "section 119(a)".

(5) Section 373 of title 35, United States Code, is amended by striking "section 119" and inserting "subsections (a) through (d) of section 119".

(6) The table of sections for chapter 11 of title 35, United States Code, is amended—

(A) by striking the item relating to section 111 and inserting the following:

"111. Application.";

and

(B) by striking the item relating to section 119 and inserting the following:

"119. Benefit of earlier filing date; right of priority.".

SEC. 533. PATENT RIGHTS.

(a) DEFINITION OF INFRINGEMENT.—Section 271 of title 35, United States Code, is amended—

(1) in subsection (a)—

(A) by inserting ", offers to sell," after "uses"; and

(B) by inserting "or imports into the United States any patented invention" after "the United States";

(2) in subsection (c), by striking "sells" and inserting "offers to sell or sells within the United States or imports into the United States";

(3) in subsection (e)—

(A) in paragraph (1), by striking "or sell" and inserting "offer to sell, or sell within the United States or import into the United States";

(B) in paragraph (3), by striking "or selling" and inserting "offering to sell, or selling within the United States or importing into the United States";

(C) in paragraph (4)(B), by striking "or sale" and inserting "offer to sell, or sale within the United States or importation into the United States"; and

(D) in paragraph (4)(C), by striking "or sale" and inserting "offer to sell, or sale within the United States or importation into the United States";

(4) in subsection (g)—

(A) by striking "sells" and inserting "offers to sell, sells,";

(B) by striking "importation, sale," and inserting "importation, offer to sell, sale,"; and

(C) by striking "other use or" and inserting "other use, offer to sell, or"; and

(5) by adding at the end the following:

"(i) As used in this section, an 'offer for sale' or an 'offer to sell' by a person other than the patentee, or any designee of the patentee, is that in which the sale will occur before the expiration of the term of the patent.".

(b) CONFORMING AMENDMENTS.—

(1) Paragraph (2) of section 41(c) of title 35, United States Code, is amended to read as follows:

"(2) A patent, the term of which has been maintained as a result of the acceptance of a payment of a maintenance fee under this subsection, shall not abridge or affect the right of any person or that person's successors in business who made, purchased, offered to sell, or used anything protected by the patent within the United States, or imported anything protected by the patent into the United States after the 6-month grace period but prior to the acceptance of a maintenance fee under this subsection, to continue the use of, to offer for sale, or to sell to others to be used, offered for sale, or sold, the specific thing so made, purchased, offered for sale, used, or imported. The court before which such matter is in question may provide for the continued manufacture, use, offer for sale, or sale of the thing made, purchased, offered for sale, or used within the United States, or imported into the United States, as specified, or for the manufacture, use, offer for sale,

EXHIBIT H

THE URUGUAY ROUND AGREEMENTS ACT

STATEMENT OF ADMINISTRATIVE ACTION

[page 656]

This Statement of Administrative Action is submitted to the Congress in compliance with section 1103 of the Omnibus Trade and Competitiveness Act of 1988 (1988 Act) and accompanies the implementing bill for the Agreement Establishing the World Trade Agreement and the agreements annexed to that Agreement (the Uruguay Round agreements). The bill approves and makes statutory changes required or appropriate to implement the Uruguay Round agreements, which the United States Trade Representative (Trade Representative) signed on April 15, 1994, on behalf of the United States under the authority of section 1102 of the 1988 Act.

This Statement describes significant administrative actions proposed to implement the Uruguay Round agreements. In addition, incorporated into this Statement are two other statements required under section 1103: (1) an explanation of how the implementing bill and proposed administrative action will change or affect existing law; and (2) a statement setting forth the reasons why the implementing bill and proposed administrative action are necessary or appropriate to carry out the Uruguay Round agreements.

As is the case with earlier Statements of Administrative Action submitted to the Congress in connection with fast-track trade bills, this Statement represents an authoritative expression by the Administration concerning its views regarding the interpretation and application of the Uruguay Round agreements, both for purposes of U.S. international obligations and domestic law. Furthermore, the Administration understands that it is the expectation of the Congress that future Administrations will observe and apply the interpretations and commitments set out in this Statement. Moreover, since this Statement will be approved by the Congress at the time it implements the Uruguay Round agreements, the interpretations of those agreements included in this Statement carry particular authority.

For ease of reference, this Statement generally follows the organization of the Uruguay Round agreements. The Statement begins with the Agreement Establishing the World Trade Organization, addresses in order each multilateral agreement contained in annexes 1 and 2 of that Agreement, and, finally, addresses the two "plurilateral" agreements that the United States will join when it enters the WTO.

In each case, the Statement first briefly summarizes the most important provisions of the particular agreement. Next, the Statement describes the pertinent provisions of the implementing bill, explaining how the bill changes or affects existing law and stating why those provisions are required or appropriate to implement the agreement. Finally, the Statement describes the administrative action proposed to implement the particular agreement, explaining how the proposed action changes existing administrative practice and stating why the changes are required or appropriate to implement the agreement.

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The Statement also addresses Title VII of the implementing bill -- the revenue provisions of the bill -- following the discussion of the two "plurilateral" agreements.

It should be noted that this Statement does not, for the most part, discuss those many instances in which U.S. law or administrative practice will remain unchanged under the Uruguay Round agreements. In many cases, U.S. laws and regulations are already in conformity with the obligations imposed by those agreements. In other cases, U.S. laws and regulations are "grandfathered" (*i.e.*, exempted) from the obligations of certain Uruguay Round agreements.

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In a few instances where there have been frequent questions from the public or the Congress, the Statement notes examples of specific statutes, regulations or practices that do *not* have to be changed as a result of the Agreement. Because this Statement is designed to describe *changes* in U.S. laws and regulations proposed to implement the Uruguay Round agreements, however, the Statement concentrates on those changes and generally does not attempt to enumerate instances in which no change in existing law or practice will be required.

Finally, references in this Statement to particular sections of U.S. statutes are based on those statutes in effect as of the date this Statement was submitted to the Congress.

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AGREEMENT ON TRADE-RELATED ASPECTS OF INTELLECTUAL PROPERTY RIGHTS

A. SUMMARY OF PROVISIONS

The Agreement on Trade-Related Aspects of Intellectual Property Rights (Agreement on TRIPs) establishes comprehensive standards for the protection of intellectual property and the enforcement of intellectual property rights in WTO member countries. It requires each WTO member country to apply the substantive obligations of the world's most important intellectual property conventions, supplements those conventions with substantial additional protection, and ensures that critical enforcement procedures will be available in each member country to safeguard intellectual property rights. The Agreement requires few changes in U.S. law and regulations and does not affect U.S. law or practice relating to parallel importation of products protected by intellectual property rights.

The Agreement is organized in seven parts. Part I deals with general principles. Part II provides standards for protection for various forms of intellectual property, copyright and neighboring rights, trademarks, geographical indications, industrial designs, patents, integrated circuit layout designs, and trade secrets. Part III regulates enforcement of intellectual property rights and Part IV deals with procedures for acquiring and maintaining such rights. Finally, the Agreement provides for dispute prevention and settlement in Part V, transitional arrangements in Part VI, and institutional and final provisions in Part VII.

1. Compliance with Multilateral Conventions

Article 2 of the Agreement requires each WTO member country to give effect to the substantive obligations of the *Paris Convention for the Protection of Industrial Property* (1967). Article 9 provides that member countries must also comply with Articles 1 through 21 and the appendix of the *Berne Convention for the Protection of Literary and Artistic Works* (1971). The United States is already a party to each of these conventions. The Agreement creates no rights or obligations with respect to authors' "moral rights" under Article 6 *bis* of the Berne Convention.

2. National Treatment and Most-Favored-Nation Treatment

Article 3 imposes a broad national treatment obligation on each WTO member country with respect to intellectual property protection. It requires each government to give "nationals" from other member countries treatment that is no less favorable than that which it gives to its own nationals with regard to the protection of intellectual property rights. The term "national" is defined by reference to the criteria for eligibility for protection under four relevant international conventions (the Paris, Berne, and Rome Conventions and the *Treaty on Intellectual Property in Respect of Protection of Integrated Circuits*). Any person or

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entity that qualifies for protection under these four conventions will be entitled to protection on a national treatment basis by all WTO member countries under the Agreement on TRIPs.

The Agreement also includes a broad most-favored-nation (MFN) obligation for each WTO member country. This provision requires each country to grant to nationals of other member countries any "advantage, favor, privilege or immunity" given to nationals of any other country with regard to the protection of intellectual property. A footnote to Article 3 makes clear that both the national treatment and MFN clauses generally confer rights with respect to all "matters affecting the availability, acquisition, scope, maintenance and enforcement of intellectual property rights as well as those matters affecting the use of intellectual property rights specifically addressed in this Agreement."

There are a few exceptions to the broad national treatment and MFN clauses. With respect to the rights of performers, producers of sound recordings, or broadcasting organizations, national treatment and MFN rights only cover the rights provided under the Agreement on TRIPs. Also, the Agreement permits member countries to continue to exercise exceptions to national treatment provided in certain international intellectual property agreements. Benefits from intellectual property agreements that enter into force prior to the WTO Agreement need not be extended on an MFN basis, nor do benefits from general agreements concerning judicial assistance or law enforcement. Finally, the procedural provisions of multilateral agreements negotiated under the auspices of the World Intellectual Property Organization, such as the Patent Cooperation Treaty, are exempt from these national treatment and MFN obligations.

3. Copyright and Related Rights

After defining the relationship between the Agreement on TRIPs and the Berne Convention, the Agreement reiterates the basic principle of copyright protection -- that protection extends only to expression and not to ideas, methods of operation, or mathematical concepts. This principle is embodied in section 102(b) of the U.S. Copyright Act (17 U.S.C. 101 *et. seq.*).

Article 10 of the Agreement confirms that all types of computer programs are "literary works" under the Berne Convention and requires each WTO country to protect them as such. It also requires copyright protection for compilations of data or other materials that are original by reason of their selection or arrangement.

Article 11 of the Agreement requires member countries to provide exclusive rental rights (the right to authorize or to prohibit commercial rental to the public of originals or copies of a work) with respect to at least computer programs and cinematographic works. WTO countries need not provide rental rights in respect of cinematographic works unless rental has led to widespread copying having a materially detrimental effect on the author's exclusive right of reproduction of the work.

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Article 12 of the Agreement provides minimum standards for the term of protection or copyrighted works. The term of protection for many works is the life of the author plus 50 years, but whenever the term of protection is not linked to the life of a person, Article 12 requires that the term be a minimum of fifty years (except for works of applied art or photographs).

Article 9:2 of the Berne Convention now bans the imposition of limitations on, or exceptions to, the reproduction right except when such limits or exceptions do not conflict with a normal exploitation of the work and do not unreasonably prejudice the legitimate interests of the right holder. Article 13 of the Agreement on TRIPs widens the scope of this provision to all exclusive rights in copyright and related rights, thus narrowly circumscribing the limitations and exceptions that WTO member countries may impose. This approach is consistent with section 107 of Copyright Act (17 U.S.C. 107) relating to fair use of copyrighted works.

Article 14 requires member countries to provide sound recording producers a fifty-year term of protection and the right to authorize or prohibit the direct or indirect reproduction and commercial rental of their sound recordings. However, a WTO member country that on April 15, 1994, had a system of payment of equitable remuneration to compensate for rental of recordings is permitted to keep that system (only Japan and Switzerland qualify under this exception).

With respect to performers, the Agreement requires WTO countries to make it possible for performers to prevent unauthorized fixation, broadcast or reproduction of their live performances. Broadcasting organizations are to be accorded similar rights, although member countries have the option of providing protection consistent with the Rome

Convention or providing owners of copyright in works broadcasted the right to prevent the same acts. The Agreement also makes Article 18 of the Berne Convention regarding the protection of existing works explicitly applicable to sound recordings.

4. Trademarks

Article 16 of the Agreement on TRIPs sets out certain basic rights that member countries must grant to the holders of a "trademark," as defined in paragraph one of Article 15. For example, the use of identical marks on identical goods and services will be presumed to create a likelihood of confusion and thus to be improper. Additionally, Article 16 requires each member country to apply the provisions of Article 6 *bis* of the Paris Convention, concerning the protection of well-known trademarks, to service marks. This Article also clarifies the standard for determining whether a trademark is "well-known."

Article 18 of the Agreement requires that the initial registration of a trademark must be for a term of not less than seven years and that the registration of a trademark must be renewable indefinitely.

Article 19 applies when a member country requires use of a trademark to maintain its registration. It provides that a trademark can be canceled for non-use only after an uninterrupted period of at least three years of non-use. However, countries must permit a trademark owner to establish the existence of circumstances beyond his control which led to the non-use of the trademark. Valid reasons for non-use, as set forth in Article 19, include import restrictions on or other government requirements for goods or services protected by the trademark. Use of a trademark by another person is recognized as use of the trademark for the purpose of maintaining a registration, if such use is controlled by the trademark owner.

Article 20 safeguards the role of a trademark as an indication of the source of the trademarked product or service by prohibiting imposition of special requirements, such as use with another trademark, that could impair this role. Member countries may, however, require the firm or person producing the goods or services to include its trademark along with, but not linked to, the trademark distinguishing the goods or services at issue.

5. Geographical Indications

Articles 22 through 24 provide for the protection of geographical indications for goods. Article 22 requires member countries to provide interested parties a means to prevent the use of product descriptions that mislead the public regarding the geographic origin of a good or that constitute "an act of unfair competition" under Article 10 *bis* of the Paris Convention. In addition, member countries must either refuse or invalidate the registration of a trademark that contains a false indication of geographic origin of the product that misleads the public. This Article also prohibits the use of a geographical indication which, although correctly reflecting the origin of the good, nonetheless falsely represents to the public that the good originates in another geographic location.

Article 23 provides additional protection for geographical indications for wines and spirits. A geographical indication for wines or spirits which does not originate in the location indicated may not be used or registered even though the true geographical origin is indicated on the product. "Homonymous geographical indications" remain protected to the extent that they do not falsely represent to the public that a good originates in another geographic location.

Article 24 specifies limited exceptions to Articles 22 and 23. First, if a trademark, which contains a geographical indication identifying wines or spirits, was used in a continuous manner with regard to the same or related goods or services for ten years before April 15, 1994, or in good faith before that date, the prohibition set forth in Article 23 is inapplicable. Secondly, a member country does not have to prevent continued and similar use of a geographical indication used on or in connection with goods or services that was

applied for or registered in good faith, or where rights have been acquired through good faith use, before the application of these provisions in that member country, or before the geographical indication is protected in its country of origin. These two provisions permit

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flexibility in expanding product lines covered by the affected trademark without jeopardizing rights in the trademark. Lastly, member countries may continue to use pre-existing grape varietal names for products of the vine, regardless of whether such names are geographical indications of another member country, provided that as of the date the WTO Agreement enters into force, the grape variety in question existed in the country permitting continued use. The principle underlying this provision also applies to the use of a person's own name or the name of his predecessor in business, except where the name is used in such a manner as to mislead the public.

Articles 23 and 24 provide for further negotiations on this subject. The Council on TRIPs, established under Article IV of the WTO Agreement, will oversee negotiations on a multilateral system of notification and registration of geographical indications for wines. Member countries will also negotiate on increased protection for individual geographical indications for wines and spirits. In these negotiations, the United States will seek improved protection for names of U.S. spirits that meet the definition of a geographical indication.

6. Industrial Designs

Articles 25 and 26 of the Agreement require each member country to provide protection for independently created industrial designs that are new or original and that meet the other conditions specified. Designs that are functional may be excluded from protection. The owner of a protected design must be given the right to prevent others from making or selling, for a commercial purpose, articles that copy or substantially copy the protected design. In addition, each government must provide a term of protection of at least ten years. Article 25 explicitly requires governments to provide protection for textile designs, either under an industrial design law or through copyright, to ensure that right owners can obtain protection without delay and unreasonable cost. Protection currently available under U.S. patent and copyright law meets the requirements of these articles.

7. Patents

a. Scope of Patentable Technology

Article 27 requires each WTO country to make patents available for inventions in all fields of technology, provided that the inventions are new, involve an inventive step (*i.e.*, are not obvious) and are capable of industrial application (*i.e.*, are useful). Governments will no longer be able to discriminate in respect to the enjoyment of patent rights based on the area of technology, place of invention, or whether the product is imported or locally made. Member countries may exclude particular inventions from patentability only in a few, narrowly defined cases.

WTO countries must make patent protection available for essentially all fields of technology, including pharmaceuticals, micro-organisms, and non-biological and microbiological processes. While they may deny patent protection for plants, they must

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provide for the protection of plant varieties either by patents or by an effective *sui generis* system or a combination of these two forms of protection. The United States provides both patent protection and plant breeder's rights. Those member countries that choose to implement a *sui generis* system of protection for plant varieties may adopt a system consistent with the *International Convention for the Protection of New Varieties of Plants* (UPOV Convention). The Agreement on TRIPs calls for the level of protection provided to plants and animals to be reviewed four years after the date of entry into force of the WTO Agreement. At that time, the United States will seek improved patent protection for plants and animals.

Special provisions apply to WTO member countries that do not already provide product patent protection for pharmaceutical and agricultural chemical products on the date the WTO Agreement enters into force. Each such country must immediately provide an interim system that permits patent applications for these products to be filed. When the application is examined, novelty will be determined as of the date of that filing. If a product is the subject of an application under this interim system, the country in question must provide exclusive marketing rights for a period of five years after the product receives marketing approval, or until a patent is granted or rejected, whichever period is shorter. To qualify for market exclusivity, the product must also be patented in another WTO member country and approved for marketing there.

b. Scope of Patent Rights

Article 28 specifies that a patent must include the right to exclude others from making, using, offering for sale, selling, or importing the product. The Agreement permits limited exceptions to the exclusive rights conferred by a patent if certain conditions are met. United States law contains some such exceptions, such as those set out in section 271(e) of the Patent Act (35 U.S.C. 271(e)).

The Agreement on TRIPs puts stringent conditions on use of a patented invention without the authorization of the right holder. This includes situations involving use of the invention by the government or use by a third party authorized by the government under a "compulsory" license. These conditions, including special conditions applicable to semiconductor technology, will also apply to compulsory licensing of rights protecting integrated circuit layout designs. Many foreign countries will be required to eliminate provisions that now subject patents to compulsory licenses if the patented invention is not produced locally.

c. Term of Protection

Article 33 requires that the term of protection available for a patent must be at least 20 years from the filing of the application. This provision permits member countries to provide for extensions of patent terms to yield patent terms that extend beyond twenty years measured from the filing date.

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d. Burden of Proof

A final provision in the Agreement's patent section addresses the allocation of the burden of proof with regard to enforcement of patents covering processes. The provision requires each member country to provide its judicial authorities with the power to order a party accused of infringing a patented process to prove that its product, if identical to the product that would stem from exercise of a patented process, was produced using a different process. The provision should facilitate the ability of a process patent holder to establish infringement.

8. Protection for Integrated Circuit Layout Designs

Articles 35 through 38 of the Agreement provide for the protection of semiconductor integrated circuit layout designs at a level fully consistent with the U.S. Semiconductor Chip Protection Act (17 U.S.C. 901, *et seq.*). They include provisions for the protection of a product incorporating a protected layout design and require innocent infringers to pay a reasonable royalty for the sell-off of stock on hand or on order when they receive notice that they are dealing with infringing designs. Article 37 makes the limitations on compulsory licenses in Article 31 applicable to layout designs. These conditions permit compulsory licensing of semiconductor technology only for public non–commercial use or to remedy an anti–competitive practice. Article 38 provides for a minimum ten–year term of protection.

9. Protection of Undisclosed Information

Article 39 requires each member country to provide protection to the holders of undisclosed information (trade secrets) provided the information is secret, has commercial value, and has been subject to reasonable steps to keep it secret. The Agreement lists some acts that constitute misappropriation of a trade secret and provides that acquisition of undisclosed information by a third party would in some cases constitute misappropriation.

Article 39 also requires member countries to protect against unfair commercial use of the information they require companies to submit to obtain marketing approval of chemical or pharmaceutical products that utilize new chemical compounds.

10. Control of Anti-Competitive Practices in Contractual Licenses

Article 40 permits member countries to adopt appropriate measures to prevent or control licensing practices or conditions that may in particular cases constitute an abuse of intellectual property rights having an adverse effect on competition in the relevant market. The Article also authorizes consultations regarding allegations of anticompetitive activity in particular cases.

11. Enforcement Procedures

Part III of the Agreement establishes extensive requirements to ensure that intellectual property rights will be effectively enforced both at and inside each member country's borders. Section 1 requires each government to provide fair and transparent enforcement procedures, including by providing intellectual property right holders access to effective judicial procedures for the enforcement of intellectual property rights. If a country provides for administrative enforcement proceedings that result in a civil remedy, Article 49 requires that those procedures conform to principles equivalent in substance to the rules set out in Section 2 for judicial procedures.

Section 2, concerning judicial procedures, requires each member country to provide for preliminary and final injunctive relief, measures to preserve evidence, civil damages, and other remedies in intellectual property enforcement proceedings. The Section also includes safeguards to protect parties from abuse of litigation procedures.

Section 3 requires member countries to establish effective procedures allowing trademark and copyright owners to obtain seizures of counterfeit and pirated goods at the border, subject to certain safeguards. For example, to protect legitimate importers, Article 55 provides that actions concerning whether goods detained at the border are infringing must be initiated within ten working days in most cases and 20 working days in appropriate cases. Such actions may be initiated by the customs authorities or any party other than the defendant in the action. Bonding requirements and improved availability of information on customs actions are important elements of this section.

Section 4 permits member countries to establish border enforcement procedures for rights other than trademark and copyright, subject to certain additional safeguards. For example, if a member country implements the border enforcement provisions of the Agreement with respect to patents, integrated circuits, trade secrets, or industrial designs, any allegedly infringing products being detained by customs authorities must be released upon payment of a bond after a specified period of time. The Section also permits customs officials to take action on their own initiative to prevent the importation of infringing goods.

Under Section 5, WTO member governments must provide criminal sanctions to address willful copyright piracy and trademark counterfeiting on a commercial scale. Criminal sanctions may also be provided to address infringement of other intellectual property rights, particularly when the infringement is willful and done on a commercial scale.

12. Acquisition and Maintenance of Intellectual Property Rights and Related Inter-Partes Procedures

Article 62 permits member countries to require compliance with reasonable procedures and formalities as a condition of acquiring or maintaining rights in patents,

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trademarks, industrial designs, geographical indications, and semiconductor mask works. With respect to intellectual property rights that are subject to registration, such as patents and trademarks, member countries must ensure that their procedures permit the grant of the right within a reasonable period of time. This rule is meant to avoid unwarranted curtailment of the term of protection. Finally, governments must provide for judicial review of final administrative decisions regarding the grant of intellectual property rights, with some minor exceptions.

13. Transparency and Dispute Settlement

Article 63 requires member countries to publish, or at least make publicly available in a national language, all laws, regulations, final judicial decisions, and administrative rulings of general application that pertain to the availability, scope, acquisition, enforcement, or prevention of the abuse of intellectual property rights. They must also publish any agreements they enter into with other WTO governments.

Article 64 makes clear that disputes arising under the Agreement on TRIPs are to be settled under the terms of the WTO Dispute Settlement Understanding. However, governments may not initiate cases against other WTO countries alleging "non-violation," nullification, or impairment of benefits under the Agreement during the first five years after the WTO Agreement goes into effect. During the five-year period, the TRIPs Council may make recommendations to the WTO Ministerial Conference concerning the appropriate scope and procedures for addressing such complaints. Approval of the recommendations or any decision to extend the five-year moratorium on bringing such cases must be made by consensus.

14. Transitional Arrangements

Articles 65 and 66 define when member countries have to meet the obligations of the Agreement on TRIPs. All member countries are given a "grace period" of one year after the entry into force of the WTO Agreement before having to apply any provisions of the Agreement on TRIPs. Any developing country, and some countries that are in the process of changing from centrally-planned to market economies, must implement the national treatment and MFN provisions after the one-year grace period but may delay implementation of all other substantive TRIPs provisions for four years after that date. An additional five-year period is available for developing countries to extend product patent protection to technologies that were not formerly eligible for protection. Least-developed country members must apply the national treatment and MFN provisions after the general one-year grace period but may delay implementation of all other TRIPs provisions for ten years from that date. The TRIPs Council may grant such countries further extensions under certain circumstances. Use of any of the transitional provisions is subject to a standstill requirement, *i.e.*, any changes made during the relevant transition period cannot result in a lesser degree of consistency with the Agreement.

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15. Institutional Arrangements and Final Provisions

Article IV of the WTO Agreement establishes a Council for TRIPs to oversee the functioning of the Agreement on TRIPs. The Agreement on TRIPs provides that the Council will monitor the operation of the Agreement including compliance matters. Article 69 provides for cooperation to eliminate trade in goods that infringe intellectual property rights, for the establishment of contact points, and for information exchanges and customs cooperation in regard to trade in counterfeit trademark and pirated copyright goods.

The TRIPs Council will review the implementation of the Agreement five years after the WTO Agreement enters into force and every two years thereafter. The Council may recommend, by consensus, that the WTO Ministerial Conference amend the Agreement to adjust to higher levels of protection of intellectual property rights already in force among all member countries.

The "final provisions" on application of the Agreement provide that no member country will have any obligations in regard to acts that occurred before that country had to apply the Agreement, but the government will be bound in respect of all subject matter existing on that date. Member countries are not required to restore protection to subject-matter that has fallen into the public domain. A reservations clause bars any reservations to the Agreement unless all other member countries consent. Finally, a general security exceptions clause permits a member country to withhold information or take action for national security reasons, or to comply with obligations under the United Nations Charter for the maintenance of international peace and security.

B. ACTION REQUIRED OR APPROPRIATE TO IMPLEMENT THE AGREEMENT

1. Implementing Bill

Title V of the implementing bill makes changes in federal law with respect to:

- rental rights in computer programs;
- protection against the unauthorized fixation in a sound recording or music video of a live performance or the communication to the public of the sounds of a live performance;
- restoration of copyright protection to works already in existence and not protected by federal copyright in the United States, but that are subject to neighboring rights or copyright protection in the WTO member country that is the source of the work;

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- the definition of "abandonment" under the trademark law;
- registrability under the trademark law of a misleading geographic indication identifying wines or spirits;
- treatment of inventive activity occurring in WTO member countries for purposes of establishing the date of invention under U.S. patent law;
- the definition of infringing activity under a patent relating to offers for sale and importation of a patented good;
- the term of protection of a patent; and
- establishment of a provisional patent application system and a right of internal priority for patent applications filed originally in the United States, as well as enabling a patent applicant to extend the term of patents that are delayed by interference proceedings, secrecy orders, and successful appeals to the Board of Patent Appeals or Interferences or a federal court.

Other areas of U.S. intellectual property law are unaffected by the Agreement on TRIPs. For example, the Agreement does not require any change in current U.S. law or practice with respect to parallel importation of goods that are the subject of intellectual property rights.

a. Rental Rights in Computer Programs

Article 11 of the Agreement requires member countries to provide exclusive "rental rights" (the right for authors or their successors in title to authorize or prohibit commercial rental to the public of originals or copies of their copyrighted works) in respect of at least computer programs and cinematographic works. Federal law provides rental rights for computer programs but those rights currently are subject to a "sunset" provision in the Computer Software Rental Amendments Act of 1990 (17 U.S.C. 109 note). Section 511 of the implementing bill eliminates the sunset provision so that authors of computer programs and their successors in title will enjoy rental rights on a permanent basis.

Article 11 also provides that member countries need not provide rental rights in respect of cinematographic works unless rental has led to widespread copying that is having a material effect on the author's exclusive right of reproduction of the work. Because the rental of motion pictures has not caused a widespread problem of copying in the United States, the bill does not provide for rental rights in respect of motion pictures.

b. Bootleg Sound Recordings and Music Videos

Article 14 of the Agreement requires WTO members to make it possible for performers to prevent the unauthorized fixation in a sound recording of their performances and to prevent the reproduction of such recordings. Various state statutes and judicial decisions presently provide criminal sanctions and civil remedies for "bootleg" recordings or reproduction of such recordings. However, these laws and decisions are not entirely uniform and may not provide the necessary basis for border enforcement against bootleg sound recordings. Sections 512 and 513 of the bill implement Article 14 of the Agreement by creating new federal civil and criminal remedies against bootlegging. These remedies will supplement, rather than preempt, state laws and judicial decisions on this subject.

Section 512 amends Title 17 of the U.S. Code to provide that bootleggers are subject to civil remedies under the Copyright Act. In addition, section 513 makes bootlegging "knowingly and for purposes of commercial advantage or private gain" a crime. It is intended that neither civil nor criminal liability will arise in cases where First Amendment principles are implicated, such as where small portions of an unauthorized fixation are used without permission in a news broadcast or for other purposes of comment or criticism.

The United States has led efforts to combat the rise in piracy of sound recordings in countries around the world. The new federal remedies will ensure that performers enjoy a high and uniform level of protection in the United States as well, and will aid efforts by the Customs Service to combat bootleg sound recordings.

c. Restoration of Copyright

Article 9 of the Agreement requires WTO countries to comply with the requirements of Article 18 of the *Berne Convention for the Protection of Literary and Artistic Works* (1971). In addition, Article 14 of the Agreement explicitly extends this requirement to sound recordings. Before the United States adhered to the Berne Convention in 1989, Congress determined that the United States was in compliance with Article 18 of the Convention but called for further study concerning whether to restore copyright protection to works from Berne Union member countries that had fallen into the public domain in the United States.

Since 1989, Congress, the Administration, the private sector, and the academic community have debated various approaches to restoring copyright protection to certain works in the public domain. The North American Free Trade Agreement Implementation Act (Pub. L. Law 103–182) took a first step by adding a new section 104A to the Copyright Act, which authorized the restoration of copyright protection to certain Mexican and Canadian motion pictures and works included in those films.

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Section 514 of the implementing bill replaces the current version of section 104A and restores protection to virtually all copyrighted works, including sound recordings, from members of the WTO or the Berne Union that are not in the public domain in their source country through the expiration of term but are not protected under copyright law in the United States. Section 514 also provides for restoring copyright to works from countries that are not WTO or Berne Union members if they provide reciprocal treatment for U.S. works. The Administration will work to ensure that other countries provide protection for U.S. works, including sound recordings, that are not in the U.S. public domain through the expiration of their term in the United States, but are in the public domain in such countries.

Section 514 provides protection to works from eligible countries if the works are not protected by copyright in the United States because:

- the copyright owner failed to comply with one or more of the formalities required by U.S. copyright law, for instance by publishing the work without a proper copyright notice, failing to renew the copyright, or by failing to comply with the manufacturing clause or *ad interim* provisions of the copyright law;

- the work is a sound recording fixed prior to February 15, 1972, and was not entitled to copyright protection; or

- the work is from a country with which the United States did not have copyright relations at the time of the work's publication.

The bill uses the term "restoration" without distinguishing between those copyrights actually "restored" by the bill and those that have never before enjoyed copyright protection in the United States. Protection is provided in both cases.

In general, copyright will be restored on the date when the TRIPs Agreement's obligations take effect for the United States, which means that the owners of restored copyrights may seek remedies against any infringements occurring on or after that date. However, section 514 includes special provisions that will apply when a "reliance party" in the United States has commenced and continued to engage in exploitation of a restored work or has acquired one or more copies or phonorecords of a restored work. The term "reliance party" also includes a person who is a successor, assignee, or licensee of another reliance party who has sold or otherwise disposed of a derivative work based upon a restored work. It further includes a person who has acquired "significant assets" of a predecessor reliance party. Reliance parties will have a 12-month grace period, after filing of constructive or receipt of actual notice that has been served by a copyright owner to enforce the restored copyright, during which the reliance party may exploit the work in any manner except for reproduction.

(1) Copyright Restoration

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Under subsection (a) of amended section 104A, copyrights in restored works will arise automatically on the date of restoration as defined in subsection (h)(2) of amended section 104A. No special steps other than those set out elsewhere in Title 17 will need to be taken to make a restored copyright fully enforceable against parties other than "reliance parties." Owners of restored copyrights will also be permitted to file for registration of the copyright simultaneously with the filing of a notice of intent to enforce a restored copyright. The notice and other formal requirements in subsections (c) through (e) of amended section 104A will apply *only* when restored copyrights are being enforced against "reliance parties."

Restored copyrights will last for the term that they would have enjoyed had they arisen and remained in force under the Copyright Act. Thus, for example:

- a French short story that was first published without copyright notice in 1935 will be treated as if it had both been published with a proper notice and properly renewed, meaning that its restored copyright will expire on December 31, 2010 (75 years after the U.S. copyright would have come into existence);

- a Chinese play from 1983 will be protected until December 31st of the fiftieth year after the year in which its author dies; or

- a Mexican sound recording first published in Mexico in 1965 will be protected until December 31, 2040.

This provision is intended to deal only with duration and does not encompass reversion or termination rights under chapters 2 and 3 of the Copyright Act.

Motion pictures and certain works included in motion pictures produced in Mexico and Canada for which copyrights were restored under the NAFTA Implementation Act will continue to enjoy copyright protection, but such protection will be governed by the new section 104A substituted by the implementing bill. Similarly, other works from NAFTA countries that are in the public domain in the United States, including motion pictures for which no NAFTA restoration was sought, will be subject to copyright restoration under the new section 104A.

(2) Ownership of a Restored Copyright

Subsection (b) of amended section 104A provides that a restored copyright is owned, in the first instance, by its author or initial right holder, as determined by the law of the restored work's "source country." This means that in certain instances it will be necessary to refer to foreign law to identify the initial owner of the restored copyright. There can be only one source country for any particular work. In the case of sound recordings, compilations, and other fixations that are "works" under U.S. law, but are

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protected by "neighboring rights" under some foreign laws, subsection (b) grants rights to the initial beneficiary of such "neighboring rights" regimes.

If the author or initial right holder at any time assigned, licensed, or otherwise alienated or disposed of an exclusive or non-exclusive interest in the copyright, that disposition is to be given effect according to the terms of the agreement, taking into account the expectations of the parties and relevant laws (including those concerning copyright, neighboring rights, contracts, descent and distribution, estates, and conflicts of law). For example, a U.S. company may have obtained rights in an underlying literary or musical work for exploitation in a motion picture "throughout the world" at a time when the underlying work was in the public domain in the United States but protected in the source country. Such a transfer would be given effect in the United States, depending on the terms of the contract as a whole.

(3) Enforcement Against "Reliance Parties"

Subsection (c) of amended section 104A provides that any owner of any exclusive interest in a restored copyright may file in the Copyright Office or serve on a reliance party a notice of intent to enforce that copyright against "reliance parties." It also makes clear that no statement or claim made in any such notice will enjoy any presumption as to its truthfulness. This provision is intended to avoid any implication that "reliance parties" (or others) face an augmented burden in contesting claims made in such notices.

The concept of "reliance party" is intended to grant, for a limited time, to persons having acted in good faith reliance on the public domain status of the now-restored work, the ability to exploit such works in most manners. It applies to two classes of persons: (1) those who acted in a certain manner prior to the date of enactment of the bill

(or, for restored works from source countries not in the Berne Union or WTO until after the WTO Agreement becomes effective with respect to the United States, the date of adherence or proclamation) and (2) those who bought or otherwise acquired an interest in restored works (or derivative works created before the date of enactment that are based on a restored work) from someone having the status of a reliance party. The first class consists of persons who either (a) engaged in acts with respect to a particular restored work, prior to the date of enactment of the Uruguay Round Agreements Act, that would have been infringing had it been copyrighted at the time (i.e., acts such as reproduction, public performance, or creation of a derivative work) *and* continued such acts after restoration, or (b) made or acquired one or more copies of a particular restored work prior to the date of enactment. Acquisition of works incorporating a material portion of a restored work are also encompassed by this provision.

The other class comprises persons who at any time either (a) bought or otherwise acquired an interest in a derivative work based upon a restored work from someone having the status of reliance party with respect to such derivative work or (b)

bought or otherwise acquired "significant assets" -- including multiple copyrights, or a back list, imprints, or tangible inventory -- from someone having the status of a reliance party.

While sometimes not technically a "reliance party," immunity from liability on like grounds is intended to be available to related parties who might otherwise be liable under doctrines such as *respondeat superior*, contributory infringement or vicarious liability, including, but not limited to, parent organizations, subsidiaries, officers, directors, shareholders, employees, agents and the like.

(4) Remedies

Subsection (d)(1) of amended section 104A provides that persons other than "reliance parties" accused of infringing restored copyrights are subject -- beginning on the date of restoration -- to full liability for acts occurring on and after that date. A restored copyright is meant to be indistinguishable from any other copyright and the holder of a restored copyright is to have exactly the same rights and remedies as any other copyright holder, except in respect to "reliance parties."

Pursuant to subsection (d)(2) of amended section 104A, no remedy may be invoked against a "reliance party" until:

- the Copyright Office has published in the Federal Register a list identifying the particular restored copyright, or
- the owner of the restored copyright serves actual notice upon the "reliance party."

Notice filed with the Copyright Office will be effective against any "reliance party," whereas actual notice will be effective with respect to the specific reliance party notified, and other reliance parties who know both of the fact of service and the contents of the notice. The Copyright Office will publish regulations that govern the filing of such notices, no later than 90 days before the TRIPs Agreement takes effect for the United States.

Any actual notice must, at a minimum, comply with the applicable provisions of subsection (e)(2) of amended section 104A, discussed below, and must be served -- whether in person or by mail -- in a manner that comports with due process. That is, "the means employed must be such as one desirous of actually informing the party might reasonably adopt to accomplish it." *Mullane v. Central Hanover Bank & Trust Co.*, 339 U.S. 306, 315 (1950). The contents of actual and constructive notices will differ in important respects because subsection (e) requires that actual notice identify the particular use to which the owner of the restored copyright objects and the work in which the restored work is used.

The "reliance party" must cease reproducing a work in which a restored copyright subsists, and cease preparing new derivative works that reproduce significant elements of a work in which a restored copyright subsists, on the date the Copyright Office publishes the title or description of the work in the *Federal Register* or the "reliance party" receives actual notice. For 12 months thereafter, however, a "reliance party" may sell off previously manufactured stock, publicly perform or publicly display the work, or authorize others to conduct these activities. The grace period will also provide an opportunity for the parties to reach a licensing agreement to permit continued use of the work. In the absence of an agreement, the reliance party must cease using the work at the end of the grace period.

Subsection (d)(3) of amended section 104A sets out additional provisions that apply to the continued exploitation, by reliance parties, of derivative works based upon restored works, where the derivative work was created prior to the date of enactment of the bill (or, for restored works from source countries not in the Berne Union or WTO until after the WTO Agreement becomes effective with respect to the United States, the date of adherence or proclamation). Such a derivative work may continue to be exploited by a relevant reliance party if the reliance party pays the owner of the restored copyright reasonable compensation. Such compensation is due in respect of any infringing conduct for which the reliance party would be liable in the absence of the provisions of subsection (d)(3).

Although it is likely that the owner of the restored copyright and the reliance party will agree on the amount of compensation to be paid, should they fail to do so, the amount of compensation would be determined by an action in federal district court, or if the parties agree, through mediation, or binding arbitration. A judge, arbitrator or mediator should set such compensation to reflect, among other things, (a) harm to the actual or potential market for or value of the restored work and (b) the relative contributions of expression of the authors of the restored work and the derivative work. In some cases, the harm to the actual or potential market of the restored work will exceed the revenue generated by the exploitation of the derivative work. Subsection (d)(3) is not intended to limit compensation due to the owner of a restored copyright in such cases.

Section 412 of the Copyright Act generally restricts the award of statutory damages and attorney's fees to copyright holders who registered their copyrights before the infringement began. Under subsection (d)(4) of amended section 104A, in the case of reliance parties, infringement will be deemed to have commenced prior to registration, so that statutory damages and attorney's fees will not be available, when activities that would have been infringing prior to the date of restoration had the restored work then been subject to copyright, were commenced prior to the date of restoration.

Remedies are available against "reliance parties" when the owner of the restored copyright has either filed constructive notice or served actual notice under subsection (d)(2) of amended section 104A. In considering whether an injunction should issue in respect of an infringement of a restored copyright, it is expected that a court would apply all of the traditional canons of equity. See *Campbell v. Acuff-Rose Music*, 114 S.Ct. 1164, 1171 n.10 (1994).

(5) Notices of Intent

Subsection (e) of amended section 104A establishes rules concerning notices of intent to enforce a restored copyright against reliance parties. First, in order to permit clear identification of the work subject to restored copyright and the owner of that right, subsection (e) specifies the minimum information that must be included in such a notice. All notices must identify the title of the restorable work in a manner that minimizes uncertainty as to the identity of the copyright that is intended to be enforced. Thus, an owner must provide English translations of foreign-language titles and alternative titles by which the work might be known of which the owner is aware. For a work, such as a photograph, that is unlikely to be known by any title it might have, the owner must describe the work to the extent necessary for its identification.

In addition, the notice must be signed by the owner of the restored copyright or his agent. An agent's signature is effective only if the owner has created the agency in writing prior to the time the agent signs the notice. Actual notice served on a "reliance party" must identify the allegedly infringing use but no such requirement exists for constructive notice filed with the Copyright Office.

The filing of a notice of intent to enforce a restored copyright shall not prejudice the ability of a person to seek at any time a judicial determination that a particular work was never in the public domain in the United States.

Subsection (e)(1) specifies certain information that must be included in constructive notices and also requires the Copyright Office to publish lists of restored copyrights that have been the subject of filings in the Copyright Office. The lists will be published quarterly and cumulated on an annual basis for two years after the relevant date of restoration for a particular country. The Administration expects that the initial 24-month period will be the relevant date of restoration for most countries, since more than 100 countries are Members of the Berne Union and many countries will be original members of the WTO when that Agreement enters into force. For countries that become "eligible countries" through adherence or proclamation, there will be a separate 24-month period for filing notices under subsection (e)(1) and the Copyright Office will publish lists of notices as specified above. The Copyright Office will keep at least one complete list of all notices published in its Public Information Office.

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Subsection (e)(3) provides that a notice will be void as to a particular restored work if it contains any knowingly false statements or claims with respect to that work. Thus, any notice listing multiple titles, one or more of which the purported owner does not in fact own or for which the copyright has not been restored, will be void in respect of such work and "reliance parties" may continue all uses until a proper notice is made.

(6) Immunity from Liability

Subsection (f)(1) of amended section 104A provides that when a party has warranted that a work containing (or based on) a restorable work does not infringe a copyright, and the warranty was made prior to January 1, 1995, that party will not be liable for breach of warranty when the breach is due solely to later restoration of the copyright. Subsection (f)(2) provides that neither the remedy of specific performance nor damages shall be available for a reliance party's failure to perform an obligation undertaken before January 1, 1995 when such performance has become infringing by virtue of restoration of a copyright under this Act.

(7) Other Provisions

Subsection (g) of amended 104A permits the President to proclaim a foreign country that is neither a member of the WTO nor of the Berne Union an "eligible country" for purposes of section 104A when that country makes restoration of copyrights available to U.S. works on substantially the same basis as that provided in the United States.

(8) Amendment to Section 109(a)

Section 514 also amends section 109(a) of the Copyright Act by adding a provision clarifying that the sale or other disposition of copies or phonorecords manufactured before the date a copyright is restored under amended section 104A, or in the case of a reliance party before publication or service of notice under 104A(e), will be authorized for purposes of direct or indirect commercial advantage only during the 12-month post-restoration grace period provided in section 104A(d).

d. Definition of "Abandonment" under the Trademark Act

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Under the current version of the Trademark Act of 1946, a mark is considered "abandoned" when its use has been discontinued with intent not to resume use. Furthermore, under the Trademark Act, non-use for two consecutive years is *prima facie* evidence of abandonment. Article 19.1 of the Agreement on TRIPs provides that a registration may be canceled only after three years of non-use. Accordingly, section 521 of the implementing bill amends section 45 of the Trademark Act to provide that three consecutive years of non-use will constitute *prima facie* evidence of abandonment. Section 521 makes no change in the provision in current law that permits a party to prove abandonment based on non-use (with intent not to resume use) during a shorter period of time.

e. Misleading Geographical Indications

Article 23.2 of the Agreement requires WTO member countries to refuse registration of any trademark consisting of a geographic indication misleadingly identifying wines or spirits or to invalidate any existing such trademark. Section 522 of the implementing bill amends section 2 of the Trademark Act of 1946 to provide that trademarks that consist of, or comprise, a geographical indication for wines or spirits that do not in fact originate in that geographic area will be refused registration if the mark was first used after the WTO Agreement has been in effect for one year. Any trademark containing a geographic indication that is currently registered or in use, or that is registered or in use during the period before the WTO Agreement has been in effect for a year, may be maintained.

As amended, section 2 of the Trademark Act will prohibit the registration of marks which contain a geographical indication which refers to a place other than where a good actually originates. "Geographical indications" are defined in TRIPs Article 22.1 as "indications which identify a good as originating in the territory of a Member, or a region or locality in that territory, where a given quality, reputation or other characteristic of the good is essentially attributable to its geographical origin." The Administration expects that this definition will be applied in the context of trademark registration and that a "geographical indication" as used in this provision will be interpreted to comprise only those areas which have a reputation for being associated with the specific goods at issue. Obscure areas or those that do not have a reputation or other characteristics generally associated with wines or spirits should not be prohibited from registration.

f. Treatment of Inventive Activity

Section 531(a) of the implementing bill amends section 104 of the Patent Act (35 U.S.C. 104). The amendment is necessary to conform to Article 27.1 of the TRIPs Agreement, which specifies that patents are to be available without discrimination as to the place of invention. These changes will permit a patent applicant or patentee to establish a date of invention only for the purposes of obtaining an invention by using evidence of inventive activity that occurs in any WTO member country.

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The ability of an inventor to establish a date of invention can be a crucial factor affecting whether the inventor can obtain patent protection in the United States. For instance, if two or more parties independently develop and seek patent protection for the same invention, the patent will be granted to the party that can establish the earlier date of invention. Under current law, no evidence can be introduced by a party seeking to prove a date of invention if the evidence is based on activity that took place outside of the United States, Canada, or Mexico. The amendment to section 104(a)(1) will remove this restriction with respect to inventive activity that occurs within WTO member countries.

The implementing bill does not change present practice regarding the effect of a determination that establishes which of two or more inventors was the first inventor. This practice precludes the losing party from separately patenting the invention in dispute, even if the invention of the winning party was not made "in this country", pursuant to application of section 102(g) of Title 35, U.S. Code. Thus, a losing party is and will continue to be

precluded through interference estoppel from separately patenting the invention in dispute or an invention that is not patently distinguishable from the invention in dispute (see *In re Deckler*, 24 U.S.P.Q.3d 1448 (Fed. Cir. 1992)).

As foreign inventive activity may now be considered in a determination of which inventor was the first to invent, fairness to both U.S. and foreign inventors demands a certain identity of treatment with regard to reliance on inventive activity in the United States and abroad. Consequently, the inability of an inventor to rely on a date of invention in the United States where the invention has been subsequently abandoned, suppressed or concealed the invention under patentability determinations under Section 102(g) should apply equally to the inventor relying on foreign inventive activity.

Section 531(a) extends existing safeguards in section 104 of Title 35 to ensure fairness to U.S. inventors. Under the current section 104(a)(3), which was added by the NAFTA Implementation Act, when a party in a proceeding before the Patent and Trademark Office, a court, or another competent authority requests information in Mexico or Canada relevant to the date of invention by an opposing party, and the information is not made available to the same extent as it could be made available in the United States, the adjudicative body must "draw appropriate inferences" or take other action permitted by statute, rule, or regulation in favor of the party that requested but could not obtain the information. The implementing bill makes this provision applicable to information in any WTO member country.

Section 531(a) also extends section 104(a)(2) to address inventive activity by individuals in government service, where the activity takes place outside their home country. Under current law, an individual in government service can rely on evidence of inventive activity outside the United States to prove a date of invention. This privilege was extended to domiciliaries of NAFTA members by the NAFTA Implementation Act. The implementing bill extends this privilege to domiciliaries of any WTO member country.

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Section 531(b) addresses the effective date of the changes to section 104. This section specifies that the changes to section 104 will apply to all patent applications filed on or later than one year after the entry into force of the WTO Agreement with respect to the United States. The provision also specifies that an applicant for patent or a patentee may not establish a date of invention that is earlier than one year after the entry into force of the WTO Agreement with respect to the United States by reference to knowledge, use or activity in a WTO country other than provided in sections 119 and 365 of Title 35.

g. Term of Patent Protection; Domestic Priority System; Provisional Applications

Under present law, the term of a U.S. patent lasts 17 years from the date of its grant, provided the required fees for maintaining the patent in force are paid. Article 33 of the Agreement requires WTO member countries to provide a patent term of at least 20 years, measured from the date the application for patent was filed.

Section 532(a) of the bill changes the manner in which the term of a U.S. patent is measured. It amends section 154 of Title 35 to provide that the term of a patent will commence on the date of issue, and end twenty years after the date on which the application resulting in the patent was filed. If priority to an earlier application or applications is claimed under sections 120, 121, or 365(c) of Title 35, the 20-year period is measured from the date of the earliest of such applications. The term of a patent that results from any application that is filed on or after the date that is six months after the effective date of this Act shall end twenty years after the date said application was filed, or if priority to an earlier application or applications is claimed under sections 120, 121 or 365(c) of Title 35, 20 years from the date of the earliest of such applications.

Section 532(a) further amends section 154 of Title 35 to provide that priority under sections 119, 365(a), or 365(b) of Title 35 is not to be taken into account in

determining the term of a patent. This provision is necessary to comply with the requirements of Article 4 *bis*(5) of the *Paris Convention for the Protection of Industrial Property* under which countries must exclude from their measurement of patent term any periods for which an applicant has based a claim of priority to an earlier foreign-filed application.

Section 532(a) also amends section 154 of Title 35 to provide for extension of the term of patents for up to a total of five years under certain circumstances. These circumstances include delays caused by interference proceedings under section 135(a), by the imposition of secrecy orders under section 181, or when a patent is issued after an adverse determination of patentability has been reversed on appeal by either the Board of Patent Appeals and Interferences or a federal court.

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In calculating the period of time of the extension of term of a patent due to an interference proceeding, the Patent and Trademark Office will include time attributable to proceedings before the Board of Patent Appeals and Interferences, as well as time before a federal court. In calculating the period of time of the extension of term under section 154(b)(2) for an appeal, section 154(b)(3)(A) directs the Patent and Trademark Office to rely on the date an appeal was taken under section 134 or 141, or an action was commenced under section 145, whichever occurs first.

The length of a patent term extension provided under the authority of section 154(b)(2) may be reduced in two instances. First, the period of patent term extension for appeal will be reduced, pursuant to section 154(b)(3)(B), for periods of time attributable to appellate review before the expiration of three years from the filing date of the application leading to the patent. Second, under section 154(b)(3)(C), an extension will be reduced for time attributable to periods during which the applicant did not act with due diligence. Although extensions under section 154(b) are limited to a total of five years, patentees will continue to be able to obtain extensions of patent term for up to five years to compensate for delays caused by pre-marketing regulatory review under the authority of existing section 156 of title 35.

A further change in U.S. law incident to the change in how patent term is measured is required by virtue of the operation of Articles 33, 70.2 and 70.4 of the TRIPs agreement. Specifically, section 532(a) of the implementing bill amends section 154 to provide that the term of a patent in force on, or that results from an application filed before, the date that is six months after the date of enactment of the Uruguay Round Agreement Act will be the greater of 17 years from the date of patent grant or 20 years from the date of filing of the application leading to the patent. A patent whose term has been disclaimed under section 253 of Title 35 due to another patent on an invention that is not patentably distinct from but was owned by or subject to an obligation of assignment to the same person shall expire on the date of the other patent. A patent whose term has been disclaimed under section 253 of Title 35 independent of another patent shall be reduced by the length of the originally disclaimed period.

Section 532(a) also adds sections 154(c)(2) and (3). These sections address situations where a third party begins use of a patented invention before the date that is six months after the date of enactment of the Uruguay Round Agreements Act and such use becomes infringing because of a change in patent term due to operation of section 154(c)(1). In such circumstances, the patent owner will not be able to obtain an injunction, recover a reasonable royalty, or obtain attorneys fees as provided for in sections 283 to 285 of Title 35, but will be able to recover equitable remuneration from a third party who infringes the patent during the period in question.

Section 532(b)(1) of the bill amends section 119 of title 35 to establish a domestic priority system. Claims to domestic priority will be made possible through use of the provisional application system established by section 532(b)(3) of the bill. Provision of a

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domestic priority right is important to ensure that applicants who file originally in the United States are not placed at a disadvantage in relation to applicants who file originally in foreign countries. As noted above, the Paris Convention precludes the United States from including in the measurement of patent term any period of time attributable to a claim for priority under 119, 365(a), or 365(b) of Title 35. The new section 119(e) extends this right to applicants that file in the United States a provisional application under section 111(b) of title 35. This will provide applicants who take advantage of this section a period of up to 12 months in which to file the formal application but claim priority based on the provisional application filed in the United States, which period will not be included in the calculation of patent term.

Section 532(b)(3) amends section 111 of title 35 to establish a provisional application system. Section 111(b) will permit an applicant to file a simplified "provisional" application for a fee of $150, or $75 for small entities, that can serve as a basis for a claim of priority if the applicant subsequently files a formal patent application within 12 months of the filing of the provisional application. The provisional application must contain a specification and any necessary drawings, in compliance with 35 U.S.C. 112 and 113, and the applicant must pay the required fee, in order to obtain a filing date for the provisional application. The provisional application need not include claims. The provisional application will not be examined, and will expire twelve months after it was filed. The inventor must present an application in compliance with all statutory requirements in order to begin the patent examination process; a provisional application cannot mature into a patent. The new section 111(b)(6) explicitly permits an applicant that has filed an application in full compliance with section 111(a) to treat said application as a provisional application under section 111(b).

Finally, section 532(c) makes conforming changes to sections 156, 172, 173, 365, and 373 of Title 35.

h. Extending the Definition of Infringing Activity

Article 28 of the Agreement sets out the rights that WTO member countries must provide through the grant of a patent. Under Article 28.1, a product patent must confer on its owner the right to prevent others from making, using, offering for sale, selling, or importing the protected invention. Under Article 28.1, a process patent must confer on its owner the right to prevent others from using the process, and from using, offering for sale, selling, or importing the product obtained directly from the process.

Under current law, a patent in the United States provides its holder the right to exclude others from making, using, or selling the invention in the United States, and to prevent importation of a product produced outside the United States using a process subject to a U.S. patent. Section 533 of the bill amends section 154 of title 35 to conform to the requirements of Article 28. This section adds to the current rights provided by section 154 the right to preclude others from offering for sale or importing a product covered by a

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United States patent. In addition, it enables the holder of a U.S. process patent to prevent others from offering to sell the products made by the patented process. Section 533 of the bill also makes appropriate conforming changes to sections 41(c)(2), 252, 262, 271, 272, 287, 292, 295 and 307 of Title 35.

2. <u>Administrative Action</u>

a. Compulsory Licensing

Article 31 of the Agreement on TRIPs limits the extent to which WTO member countries may grant "compulsory licenses," that is, permit the use by the government or third parties of a patented product or process without the patent owner's

permission. The article sets out a number of conditions a government must meet before granting such a license.

U.S. law currently provides for the issuance of compulsory licenses under three statutes -- the Atomic Energy Act, the Clean Air Act, and the Energy Policy Act (which amended the Atomic Energy Act). Regulations governing the grant of compulsory licenses under each of these statutes currently require satisfaction of all of the conditions set out in Article 31 except the requirement in paragraph (c), which specifies that compulsory licenses on semiconductor technology may be granted only for a public non-commercial use or to remedy an anticompetitive practice.

The Department of Energy will modify regulations set out at 10 CFR Part 780, and the Environmental Protection Agency will amend its regulations implementing section 308 of the Clean Air Act, to meet the requirements of Article 31(c) for any compulsory licenses they issue in respect of semiconductor technology or designs. In addition, the President will issue an Executive Order ensuring that all government agencies that may invoke "government use" provisions meet those requirements as well.

b. Patent Applications

To facilitate the completion of prosecution of applications pending in the Patent and Trademark Office as of the effective date of section 154(a)(2), section 532(a)(2) directs the Commissioner of Patents and Trademarks to establish regulations for two purposes.

The first purpose is to provide for further limited reexamination of an application pending for two years or longer as of the effective date of section 154(a)(2) of title 35, taking into account any reference made in such application to any earlier filed application under sections 120, 121 or 365(c) of title 35. The further limited reexamination will permit applicants to present for consideration a submission after the Patent and Trademark Office has issued a final rejection on an application.

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The types of submissions shall include, but shall not be limited to, an information disclosure statement, an amendment to the specification or claims, or new substantive arguments or new evidence in support of patentability of the claimed invention. The Patent and Trademark Office will consider on the merits the first and second such submissions, to the extent that such submissions would have been entitled to consideration if made prior to final rejection. The Patent and Trademark Office will modify such final rejection or allow such application, as appropriate, based on the consideration of such submissions. As is current practice, the Patent and Trademark Office shall consider any submission which, in the opinion of the Patent and Trademark Office, places the application in condition for allowance or in better condition for appeal. The Commissioner will determine an appropriate fee, related to the reexamination provided, for the filing of such submissions.

The second purpose for the new regulations is to address Patent and Trademark Office restriction requirements and filings of divisional applications, and to ensure that there is an opportunity for an applicant to respond to a requirement for restriction or for the filing of a divisional application. After the effective date of section 154(a)(2), the Patent and Trademark Office will not make or maintain a requirement for restriction or the filing of a divisional application for an application that has been pending for three years or longer as of the effective date of said section, taking into account any reference made in such application to any earlier filed application under sections 120, 121 or 365(c) of title 35. This limitation does not apply if such a requirement was first made in such application or a predecessor application more than two months prior to such effective date, or if there has not been at least one Patent and Trademark Office action due to actions by the applicant. The Commissioner will determine an appropriate fee for examination of each independent and distinct invention in an application in excess of one.

Measuring the term of a patent from the filing date of the patent application instead of from the date of grant of the patent increases the importance of expeditious processing of applications by the Patent and Trademark Office. The Administration continues to be committed to working with the Congress to ensure that adequate resources are available for prompt processing of all patent applications. The Patent and Trademark Office will continue its efforts to hire and retain sufficient numbers of highly qualified examiners to enable it to handle the increasing number of applications being filed in complex technological areas, such as biotechnology, computers, and software. The Patent and Trademark Office will also continue its efforts to provide adequate legal and technical training for its examiners to ensure that the patent examining corps is equipped to handle increasingly complex patent applications expeditiously.

Some in industry have expressed concerns over possible sources of delay during examination of patents that could lead to a decrease in effective patent term. Such concerns focus on the Office's application of the utility requirement during examination of patent applications claiming pharmaceutical inventions. Under U.S. law, if a patent application contains a disclosure of utility that corresponds in scope to the subject matter

sought to be patented, the specification must be taken as sufficient to satisfy the utility requirement of section 101 of title 35 for the entire claimed subject matter, unless there is reason for one skilled in the art to question the objective truth of the statement of utility or its scope. If the Office rejects an application on the grounds that the invention lacks utility, the applicant may provide evidence supporting the truth of the statement of utility and its scope as found in the specification. If the evidence is persuasive, a rejection for lack of utility may be overcome. An applicant may satisfy the utility requirement for a pharmaceutical invention by demonstrating evidence of pharmacological activity in either *in vitro* or *in vivo* experiments such that a person skilled in that field would conclude that utility has been established. Under most circumstances, human clinical data is not necessary to establish utility. And, to ensure that concerns related to utility are fully addressed, the Patent and Trademark Office will sponsor a public hearing to ascertain whether patentees claiming protection for biotechnological inventions lose effective patent term in the course of developing evidence to establish that such inventions are in fact useful.

c. Geographical Indications

The United States will implement the Agreement's provisions on geographical indications for wine and spirits through the labeling regulations of the Bureau of Alcohol, Tobacco and Firearms of the Department of the Treasury. The Agreement specifically recognizes that rights in geographic indications for wine and spirits may be enforced through administrative action.

d. Border Enforcement

The Agreement on TRIPs contains detailed provisions on border enforcement against imports of pirated and counterfeit goods. Although U.S. law and customs regulations already meet the minimum TRIPs requirements, current customs regulations do not provide for uniform procedures in the treatment of copyright and trademark infringement actions. The Customs Service will issue revised regulations to harmonize those requirements.

EXHIBIT I

(7) URUGUAY ROUND AGREEMENTS.—The term "Uruguay Round Agreements" means the agreements approved by the Congress under section 101(a)(1).

(8) WORLD TRADE ORGANIZATION AND WTO.—The terms "World Trade Organization" and "WTO" mean the organization established pursuant to the WTO Agreement.

(9) WTO AGREEMENT.—The term "WTO Agreement" means the Agreement Establishing the World Trade Organization entered into on April 15, 1994.

(10) WTO MEMBER AND WTO MEMBER COUNTRY.—The terms "WTO member" and "WTO member country" mean a state, or separate customs territory (within the meaning of Article XII of the WTO Agreement), with respect to which the United States applies the WTO Agreement.

TITLE I—APPROVAL OF, AND GENERAL PROVISIONS RELATING TO, THE URUGUAY ROUND AGREEMENTS

Subtitle A—Approval of Agreements and Related Provisions

19 USC 3511.

SEC. 101. APPROVAL AND ENTRY INTO FORCE OF THE URUGUAY ROUND AGREEMENTS.

(a) APPROVAL OF AGREEMENTS AND STATEMENT OF ADMINISTRATIVE ACTION.—Pursuant to section 1103 of the Omnibus Trade and Competitiveness Act of 1988 (19 U.S.C. 2903) and section 151 of the Trade Act of 1974 (19 U.S.C. 2191), the Congress approves—

(1) the trade agreements described in subsection (d) resulting from the Uruguay Round of multilateral trade negotiations under the auspices of the General Agreement on Tariffs and Trade, entered into on April 15, 1994, and submitted to the Congress on September 27, 1994; and

(2) the statement of administrative action proposed to implement the agreements that was submitted to the Congress on September 27, 1994.

(b) ENTRY INTO FORCE.—At such time as the President determines that a sufficient number of foreign countries are accepting the obligations of the Uruguay Round Agreements, in accordance with article XIV of the WTO Agreement, to ensure the effective operation of, and adequate benefits for the United States under, those Agreements, the President may accept the Uruguay Round Agreements and implement article VIII of the WTO Agreement.

(c) AUTHORIZATION OF APPROPRIATIONS.—There are authorized to be appropriated annually such sums as may be necessary for the payment by the United States of its share of the expenses of the WTO.

(d) TRADE AGREEMENTS TO WHICH THIS ACT APPLIES.—Subsection (a) applies to the WTO Agreement and to the following agreements annexed to that Agreement:

(1) The General Agreement on Tariffs and Trade 1994.

(2) The Agreement on Agriculture.

EXHIBIT J

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO.: 4,626,538

DATED: December 2, 1986

INVENTOR(S): Dusza et al.

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

On the face of the patent, cancel at [*] Notice: "The portion of the term of this patent subsequent to Jun. 3, 2002, has been disclaimed."

and substitute

The portion of the term of this patent subsequent to the expiration date of U.S. Patent No. 4,521,422 has been disclaimed.

Mailing Address of Sender:

Finnegan, Henderson, Farabow
Garrett & Dunner, L.L.P.
1300 I Street, N.W.
Washington, DC 20005-3315

FORM PTO 1050 (Rev.2-93)

PATENT NO. 4,626,538

No. of add'l copies
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➡ _____

EXHIBIT K

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
ASSISTANT SECRETARY AND COMMISSIONER
OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

Paper No. 25

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SPECIAL PROGRAMS OFFICE
OAC FOR PATENTS

THOMAS SARRO
LARSON AND TAYLOR
SUITE 900
1199 NORTH FAIRFAX STREET
ALEXANDRIA, VIRGINIA 22314

In re Patent No: 4,346,116 :
Application No. 06/151,816 :
Filed: October 31, 1984 : DECISION DENYING PETITION
Issue date: August 24, 1982 :
Inventor: Francoise Verwaerde et al:

This is a decision on the renewed petition under 37 CFR 1.182, which now requests that the PTO "give notice to the public of the true expiration date of the patent, i.e., May 14, 1999."

The petition is DENIED.

BACKGROUND

In response to the final Office action of August 19, 1991 , wherein the examiner rejected inter alia, various claims over claims 6 and 7 of copending application No. 038,711, applicants filed an amendment and a terminal disclaimer on December 21, 1981. The accompanying remarks noted:

> "[t]he amendment (sic, rejection) of claims 27-34 and 37-40 as obvious variants of claims in Serial No. 038,711 is being obviated by the Terminal Disclaimer submitted herewith."

The application was allowed by the examiner in the Office communication mailed March 15, 1992, and issued August 24, 1982.

A petition filed September 11, 1997, requested under 37 CFR 1.182 that the recorded terminal disclaimer filed on December 21, 1981, be withdrawn in favor of a revised, apparently forthcoming, terminal disclaimer, and further, that a Certificate of Correction (PTO mistake) be issued to that effect. Petitioners specifically requested that the aforementioned original terminal disclaimer be replaced, in that the instant patent term, via the original terminal disclaimer, is limited to the pre "GATT-NAFTA" (Uruguay

Round Agreements Act (URAA) (1994)) expiration date for U.S. Patent No. 4,279,931 (July 21, 1998), while the latter patent now expires May 14, 1999, as was apparently to be reflected in any forthcoming terminal disclaimer. As such, petitioner asserted, the instant patent contains an erroneous date of expiration, and further, as the error in the patent is not the fault of petitioner, no fees for either the petition, or the requested Certificate of Correction, should be assessed.

The petition was dismissed in the decision of February 11, 1998.

The instant renewed petition was filed April 13, 1998.

STATUTE AND REGULATION

35 USC § 253 states that:

> Whenever, without any deceptive intention, a claim of a patent is invalid the remaining claims shall not thereby be rendered invalid. A patentee, whether of the whole or any sectional interest therein, may, on payment of the fee required by law, make disclaimer of any complete claim, stating therein the extent of his interest in such patent. disclaimer shall be in writing, and recorded in the Patent and Trademark Office; and it shall thereafter be considered as part of the original patent to the extent of the interest possessed by the disclaimant and by those claiming under him.
>
> In like manner any patentee or applicant may disclaim or dedicate to the public the entire term, or any terminal part of the term, of the patent granted or to be granted.

35 USC § 254 provides:

> Whenever a mistake in a patent, incurred through the fault of the Patent and Trademark Office, is clearly disclosed by the records of the Office, the Commissioner may issue a certificate of correction stating the fact and nature of such mistake, under seal, without charge, to be recorded in the records of patents. A printed copy thereof shall be attached to each printed copy of the patent, and such certificate shall be considered as part of the original patent. Every such patent, together with such certificate, shall have the same effect and operation in law on the trial of actions for causes thereafter arising as if the same had been originally issued in such corrected form. The Commissioner may issue a

corrected patent without charge in lieu of and with like effect as a certificate of correction.

35 USC § 255 states that:

> Whenever a mistake of a clerical or typographical nature, or of minor character, which was not the fault of the Patent and Trademark Office, appears in a patent and a showing has been made that such mistake occurred in good faith, the Commissioner may, upon payment of the required fee, issue a certificate of correction, if the correction does not involve such changes in the patent as would constitute new matter or would require re-examination. Such patent, together with the certificate, shall have the same effect and operation in law on the trial of actions for causes thereafter arising as if the same had been originally issued in such corrected form.

37 CFR 1.182 provides that:

> All situations not specifically provided for in the regulations of this part will be decided in accordance with the merits of each situation by or under the authority of the Commissioner, subject to such other requirements as may be imposed, and such decision will be communicated to the interested parties in writing. Any petition seeking a decision under this section must be accompanied by the petition fee set forth in § 1.17(h).

37 CFR 1.322 provides that:

> (a) A certificate of correction under 35 U.S.C. 254 may be issued at the request of the patentee or the patentee's assignee. Such certificate will not be issued at the request or suggestion of anyone not owning an interest in the patent, nor on motion of the Office, without first notifying the patentee (including any assignee of record) and affording the patentee an opportunity to be heard. When the request relates to a patent involved in an interference, the request shall comply with the requirements of this section and shall be accompanied by a motion under § 1.635.
>
> (b) If the nature of the mistake on the part of the Office is such that a certificate of correction is deemed inappropriate in form, the Commissioner may issue a corrected patent in

lieu thereof as a more appropriate form for certificate of correction, without expense to the patentee.

37 CFR 1.321 states:

(a) A patentee owning the whole or any sectional interest in a patent may disclaim any complete claim or claims in a patent. In like manner any patentee may disclaim or dedicate to the public the entire term, or any terminal part of the term, of the patent granted. Such disclaimer is binding upon the grantee and its successors or assigns. A notice of the disclaimer is published in the Official Gazette and attached to the printed copies of the specification. The disclaimer, to be recorded in the Patent and Trademark Office, must:

(1) be signed by the patentee, or an attorney or agent of record;

(2) identify the patent and complete claim or claims, or term being disclaimed. A disclaimer which is not a disclaimer of a complete claim or claims, or term, will be refused recordation;

(3) state the present extent of patentee's ownership interest in the patent; and

(4) be accompanied by the fee set forth in § 1.20(d).

(b) An applicant or assignee may disclaim or dedicate to the public the entire term, or any terminal part of the term, of a patent to be granted. Such terminal disclaimer is binding upon the grantee and its successors or assigns. The terminal disclaimer, to be recorded in the Patent and Trademark Office, must:

(1) be signed:

(i) by the applicant, or

(ii) if there is an assignee of record of an undivided part interest, by the applicant and such assignee, or

(iii) if there is an assignee of record of the entire interest, by such assignee, or

(iv) by an attorney or agent of record;

(2) specify the portion of the term of the patent being disclaimed;

(3) state the present extent of applicant's or assignee's ownership interest in the patent to be granted; and

(4) be accompanied by the fee set forth in § 1.20(d).

(c) A terminal disclaimer, when filed to obviate a judicially created double patenting rejection in a patent application or in a reexamination proceeding, must:

(1) Comply with the provisions of paragraphs (b)(2) through (b)(4) of this section;

(2) Be signed in accordance with paragraph (b)(1) of this section if filed in a patent application or in accordance with paragraph (a)(1) of this section if filed in a reexamination proceeding; and

(3) Include a provision that any patent granted on that application or any patent subject to the reexamination proceeding shall be enforceable only for and during such period that said patent is commonly owned with the application or patent which formed the basis for the rejection.

(c) A terminal disclaimer, when filed to obviate a judicially created double patenting rejection in a patent application or in a reexamination proceeding, must:

(1) Comply with the provisions of paragraphs (b)(2) through (b)(4) of this section;

(2) Be signed in accordance with paragraph (b)(1) of this section if filed in a patent application or in accordance with paragraph (a)(1) of this section if filed in a reexamination proceeding; and

(3) Include a provision that any patent granted on that application or any patent subject to the reexamination proceeding shall be enforceable only for and during such period that said patent is commonly owned with the application or patent which formed the basis for the rejection.

37 CFR 1.323 states that:

> Whenever a mistake of a clerical or typographical nature or of minor character which was not the fault of the Office, appears in a patent and a showing is made that such mistake occurred in good faith, the Commissioner may, upon payment of the fee set forth in § 1.20(a), issue a certificate, if the correction does not involve such changes in the patent as would constitute new matter or would require reexamination. A for a certificate of correction of a patent involved in an interference shall comply with the requirements of this section and shall be accompanied by a motion under § 1.635.

OPINION

Petitioners request reconsideration in that the decision of February 11, 1998 is asserted to have failed to address the basis of the prior request filed September 11, 1997. Specifically petitioners assert, the Commissioner has authority under 37 CFR 1.182 to give notice to the public of the true expiration date of the above-captioned patent, which petitioner contends, is May 14, 1999.

The showing of record fails to adequately demonstrate that the facts of this case warrant the relief(s) requested.

The terminal disclaimer under 35 USC § 253 and 37 CFR 1.321, filed December 21, 1981, was relied upon by petitioners to overcome a rejection on the grounds of obviousness type double patenting involving the claims of commonly owned U. S. Patent No. 4,279,931 issued July 21, 1981. The terminal disclaimer was executed by Germain Roquette, on behalf of the assignee, Roquette Freres, and specified in pertinent part that:

> "The said assignee does hereby disclaim and dedicate to the public the terminal portion of any United States Patent to be issued on this application beyond July 21, 1998."

While petitioners now predicate their request for withdrawal of the recorded terminal disclaimer upon a subsequent change in the term of the '931 patent, inspection of the above-quoted language in that disclaimer reveals that petitioners originally made such disclaimer contingent upon an actual date of expiration of the term of the '931 patent. That is, petitioners made the original terminal disclaimer absolute, that is, date-specific to July 21, 1998. It follows that regardless of what effect the URAA may have

subsequently had on the expiration date of the '931 patent, there is no nexus between that date and the specific expiration date as set forth in the original terminal disclaimer of record. As such, no error is apparent in the term of the original instant letters patent, as indicated by the recorded terminal disclaimer, which warrants correction. As such, it is not apparent from the record, and petitioner has not shown, on the record, how the express date certain patent expiration of July 21, 1998 given by the assignee of the entire interest, becomes May 14, 1999. Rather, as the patent was freely stated to expire on July 21, 1998 whatever effects the URAA might have had on the term of other patent, is simply immaterial to the date specific expiration of the above-captioned patent. Contrary to petitioners' contention, whatever authority may be vested under and by the patent statutes and rules of practice, such authority does not controvert the assignee's express statement of a date certain expiration of the instant patent. In other words, it is manifestly inconsistent with the express language supplied by petitioners in the above-noted terminal disclaimer to now aver that the "true expiration date" is any other than that specifically recited in the terminal disclaimer, and proclaimed to the public as part of the instant patent since its date of issuance.

It is also brought to petitioners' attention that:

> "The purpose of the URAA [codified in part in 35 U.S.C. § 154] **was not to extend patent terms**, although it has that effect in some cases, but to harmonize the term provision of United States patent law with that of our leading trading partners which grant a patent term of 20 years from the date of filing of the patent application. Prior to June 8, 1995, U.S. patents had an expiration date under 35 U.S.C. Section 154 **measured as 17 years from the date the patent issued, except where terminal disclaimers were filed.** Amended section 154(a) now reads:
>
> > Subject to the payment of fees under this title, such grant shall be for a term beginning on the date on which the patent issues and ending 20 years from the date on which the application for the patent was filed in the United States or, if the application contains a specific reference to an earlier filed application or applications under section 120, 121, or 365(c) of this title, from the date on which the earliest such application was filed.

35 U.S.C. § 154(a)(2) (1994).

For certain patents which were issued and for pending applications which were filed prior to June 8, 1995, a transitional provision preserves a guaranteed 17-year term, if it is longer than 20 years from filing, by the following provision:

> The term of a patent that is in force on or that results from an application filed before the date that is 6 months after the date of the enactment of the Uruguay Round Agreements Act **shall be the greater of the 20-year term as provided in subsection (1), or 17 years from grant, subject to any terminal disclaimers.**

Id. at Section 154(c)(1). Patents in the section 154(c)(1) category thus are entitled to keep or to enjoy the 17-year term from issuance of the patent or a 20-year from filing term, whichever is longer."[1] (emphasis added)

The statutory authority for amendment or correction of an issued patent is found in title 35, chapter 25. The instant petition does not involve correction of a mistake by the Patent and Trademark Office (Office) (35 USC § 254) or correction of the named inventor (35 USC § 256). In addition, while the instant petition involves a disclaimer, 35 USC § 253 merely authorizes the filing and recording of disclaimers; it does not authorize the withdrawal of a terminal disclaimer. Finally, petitioners have not sought amendment or correction by reissue (35 USC §§ 251 and 252).

Unless a "mistake" is provided for in 37 CFR 1.322, 1.323, or 1.324, or affords legal grounds for reissue or for reexamination, such "mistake" will not be corrected subsequent to the issuance of an application as a patent. See 37 CFR 1.325. As stated in section 1490 of the Manual of Patent Examining Procedure (MPEP) (6th Ed., Rev. 3 1997), the mechanisms to correct a patent (i.e., certificate of correction (35 USC § 255), reissue (35 USC § 251) and reexamination (35 USC § 305)) are not available to withdraw or otherwise nullify the effect of a recorded terminal disclaimer.

---

[1] Merck & Co. v. Kessler, 80 F.3d 1543, 1547-1548, 38 USPQ2d 1347, 1349-1350 (Fed. Cir. 1996).

Further in this regard, the public has had fifteen (fifteen) years since the grant of the above-identified patent, to act on its facial representation that the term of this patent will expire, at the latest, on July 21, 1998. Similarly, petitioners have had, since the submission of the aforementioned terminal disclaimer on December 21, 1981, no reasonable basis to expect a term for this patent that would extend beyond July 21, 1998.

While petitioners may now consider the originally filed disclaimer to be unnecessary, or unnecessarily limiting, petitioners are, nevertheless, confronted with what has been characterized as "an unhappy circumstance", rather than a circumstance necessitating relief. See In re Jentoft, 392 F.2d 633, 639 n. 6, 157 USPQ 363, 368 n. 6 (CCPA 1968); MPEP 1490. When the question of whether or not a given set of claims in one application or patent is distinct from another set of claims in another application or patent with respect to obviousness double patenting arises, that question relates to the merits of an invention, and the appropriate remedy for resolution of that issue ultimately lies by appeal as provided by statute. See e.g. In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Petitioners had the opportunity to challenge the need for a terminal disclaimer, on appeal, but instead, freely chose to file a terminal disclaimer to avoid the rejection, during the prosecution of the application that led to the above-identified patent. Such does not afford proper legal or public policy grounds for requesting nullification of the terms of free dedication to the public contained in the previously filed terminal disclaimer by way of appeal, much less on petition. Cf. Ex Parte Anthony, 230 USPQ 467 (PBAI 1982) aff'd. No. 84-1357 (Fed. Cir. June 14, 1985).

Even assuming, *arguendo*, the relief(s) requested should be considered on petition, petitioners are reminded that, as a general rule, public policy does not favor the restoration to the patentee [applicant] of something that has been freely dedicated to the public, particularly where the public interest is not protected in some manner, e.g., intervening rights in the case of a reissue patent. See Altoona Publix Theatres v. American Tri-Ergon Corp., 294 U.S. 477, 24 USPQ 308 (1935). Petitioners have failed to provide a reasonable, much less any, assurance that the public interest will, or can be, protected if the relief(s) requested in this petition are given favorable consideration. In this regard, an applicant's use, and Office acceptance, of a terminal disclaimer is in the public interest because such encourages the disclosure of additional developments, the earlier filing of patent applications, and the earlier expiration of

patents whereby the inventions covered become freely available to the public. Jentoft, supra. It is brought to petitioners' attention that the principle against recapturing something that has been intentionally dedicated to the public dates back at least to Leggett v. Avery, 101 U.S. 246 (1879). As noted above, while petitioners may now consider the previously filed disclaimer to be unnecessary, or unnecessarily limiting, petitioners are, nevertheless, confronted with what has been characterized as "an unhappy circumstance", rather than a circumstance(s) necessitating relief. Jentoft at 639 n. 6, 157 USPQ at 368 n. 6.

Moreover, petitioners have made no attempt to explain their delay in presenting this petition, over two years after the implementation of the URAA. The public has thus had some two years within which to rely on the fact that, notwithstanding the URAA of 1994, and its effective date of June 8, 1995, petitioners permitted the original terminal disclaimer in this patent to continue in unabated force and effect. While petitioners should not infer that, had the instant petition been more seasonably presented, a different result might have been obtained; nevertheless, the record shows that petitioners did not diligently address the issues pertaining to the instant terminal disclaimer presented by the aforementioned URAA. Assuming, *arguendo*, that petitioners may, seasonably or otherwise, request rescission of the terminal disclaimer of record, equitable powers should not be invoked to excuse the performance of a condition by a party that has not acted with reasonable, due care and diligence. U.S. v. Lockheed Petroleum Services, 709 F.2d 1472, 1475 (Fed. Cir. 1983).

In any event, to withdraw the recorded terminal disclaimer filed on December 21, 1981 and properly recorded in the above-identified patent, such action must be authorized pursuant to 35 USC § 255.

A Certificate of Correction under 35 USC § 255 and 37 CFR 1.323 is available for the correction of errors of a minor or clerical character, and does not extend to the correction of errors that would constitute new matter or would require reexamination. See In re Arnott, 19 USPQ2d 1049, 1054 (Comm'r Pat. 1991); In re Hyman, 185 USPQ 441, 442 (Sol. Pat. 1975). Specifically, 35 USC § 255 requires, *inter alia*, that two specific and separate requirements be met prior to the issuance of a Certificate of Correction. The first requirement is that the mistake is: (1) of a clerical nature, (2) of a typographical nature, or (3) of minor character. The second requirement is that the correction must not involve changes that would: (1) constitute new matter or (2) would

require reexamination. See Arnott 19 USPQ2d at 1052; see also MPEP 1490.

Apparently, the "mistake" at issue here involves petitioners' inclusion in the terminal disclaimer filed December 21, 1981, of a specific expiration date: July 21, 1998. However, this "mistake" is not one of a clerical or typographical nature; rather correcting this "mistake" would involve a substantive change to the recorded terminal disclaimer of record. Secondly, the "broadening" of the claims of a patent, via the attempted removal of a recorded terminal disclaimer, requires reexamination (pursuant to 35 USC § 251) of the issues raised thereby. See Anthony, supra. Further, in this regard, even while 35 USC 251 is a remedial statute, and, as such, is often liberally construed, nevertheless, there is a two year bar on any remedy that would effectuate broadening of an issued patent. See 35 USC 251. As held in Anthony, however, removal of a recorded terminal disclaimer, and the resultant "broadening" of the vertical scope (term) of the original patent, is prohibited, *inter alia*, if the attempt via reissue is not sought within two years of the patent grant. See id. at 470. It would appear to be an improper exercise of 37 CFR 1.182 to permit petitioner to regain, on petition, what petitioner could not herein regain under the remedial patent statute, which, as such, is "liberally construed." Under the facts of this case, it would be an inappropriate exercise of 37 CFR 1.182 to rescind the terminal disclaimer.

DECISION

For the reasons given above, it would be an inappropriate exercise of 37 CFR 1.182 to rescind the terminal disclaimer of record. Accordingly, the petition is granted to the extent that the previous decision has been reconsidered, but is **denied** as to rescinding the terminal disclaimer of record.

This patent file is being returned to the Files Repository.

Telephone inquiries relative to this decision should be directed to Special Projects Examiner Brian Hearn at (703) 305-1820.

Manuel A. Antonakas
Director, Office of Patent Policy Dissemination
Office of the Deputy Assistant Commissioner
for Patent Policy and Projects

EXHIBIT L

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
ASSISTANT SECRETARY AND COMMISSIONER
OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

Paper No. 24

KEIL & WEINKAUF
1101 CONNECTICUT AVENUE, N.W.
WASHINGTON, D.C. 20036

In re Patent No: 4,654,073 :
Application No. 06/666,908 :
Filed: October 31, 1984 : DECISION GRANTING PETITION
Issue date: March 31, 1987 :
Inventor: Dieter Jahn et al. :

This is a decision on the renewed petition filed March 9, 1998, under 37 CFR 1.182, that the recorded terminal disclaimer filed on March 14, 1986, be withdrawn in favor of the terminal disclaimer filed with the petition, and further, that a Certificate of Correction (PTO mistake) be issued to that effect.

The petition is granted to the extent indicated below.

Petitioner again requests that the aforementioned original terminal disclaimer be replaced with that filed August 27, 1997 in that the instant patent term, via the original terminal disclaimer, is limited to the pre "GATT-NAFTA" (i.e., the Uruguay Round Agreements Act (URAA) (1994)) expiration date for U.S. Patent No. 4,422,864 (December 27, 2000), while the latter patent now expires May 20, 2002, as reflected in the newly proffered terminal disclaimer. As such, petitioner asserts, the instant patent contains an erroneous date of expiration, and further, as the error in the patent is not the fault of petitioner, no fees for either the petition, or the requested Certificate of Correction, should be assessed.

The terminal disclaimer filed under 35 USC § 253 and 37 CFR 1.321(c) on March 14, 1986, was relied upon by petitioner to overcome a rejection on the grounds of obviousness-type double patenting involving the claims of commonly owned U. S. Patent No. 4,442,864. The terminal disclaimer was executed by Messrs. Raemisch and Richters, on behalf of the assignee, BASF Aktiengesellschaft, and specified in pertinent part that:

> "Your Petitioner, by two duly authorized representatives, hereby disclaims the terminal part of any patent granted on the above-identified application which would extend beyond the expiration date of United States Patent No. 4,422,864 **(expiration date December 27, 2000)**, which is also owned by petitioner...[emphasis added]"

At the time the instant patent was published, the PTO printed thereon the specific expiration date, i.e., December 27, 2000, of U.S. Patent No. 4,422,864 as the end of the term of the instant patent as such date was then identical to the "expiration date," notwithstanding petitioner's concurrent use of the relative term "the expiration date of United States Patent No. 4,422,864."

Due to the changes to 35 U.S.C. § 154(c)(1) contained in Public Law 103-465, § 532, 108 Stat. 4809 (1994), the expiration date of U.S. Patent No. 4,422,864 (as well as the instant patent) is not December 27, 2000; rather it is now May 20, 2002, as correctly noted by petitioner. Thus, the terminal disclaimer of March 14, 1986 creates an ambiguity, in that it sets forth two (2) dates beyond which the terminal date of the above-identified patent is disclaimed: December 27, 2000, and May 20, 2002.

However, in order to resolve the ambiguity in the aforementioned terminal disclaimer filed on March 14, 1986 created by the changes to 35 U.S.C. 154(c)(1) contained in Public Law 103-465, it is not necessary, as requested by petitioner, to substitute the proffered terminal disclaimer for that already recorded. Rather, the correction of the terminal disclaimer date indicated on a patent due to the changes to 35 U.S.C. § 154 contained in Public Law 103-465, § 532, 108 Stat. 4809 (1994) is, if such correction is appropriate, by way of 35 U.S.C. § 254 and 37 CFR 1.322. However, in light of possible future changes to the patent statutes, the proffered Certificate of Correction, as it also recites a specific expiration date, might tend to replicate the problem already encountered herein. As such, the proffered Certificate of Correction will not be accepted.

Nevertheless, the instant file is being forwarded to Certificates of Correction Branch for issuance of a Certificate of Correction to now indicate that, in lieu of the former statement pertaining to the expiration of the term by way of a terminal disclaimer :

--[*] Notice: This patent is subject to a terminal disclaimer.--

Telephone inquiries relative to this decision should be directed to the undersigned at (703) 305-1820.

Brian Hearn
Special Projects Examiner
Office of Petitions
Office of the Deputy Assistant Commissioner
for Patent Policy and Projects

PATENT
Atty. Docket No.: 1142.0068-00

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re U.S. Patent No. 4,626,538)
Issued: December 2, 1986)
To: John P. Dusza,)
Andrew S. Tomcufcik,)
Jay D. Albright)
Assignee: American Cyanamid Company)
For: [7-(3-DISUBSTITUTED AMINO)PHENYL])
PYRAZOLA[1,5-A]PYRIMIDINES)

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

POWER OF ATTORNEY
AND STATEMENT UNDER 37 C.F.R. § 3.73(b)

Assignee, American Cyanamid Company, being the owner of the above-identified U.S. Letters Patent, hereby grants the power of attorney to **FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER, L.L.P., Reg. No. 22,540,Douglas B. Henderson, Reg. No. 20,291; Ford F. Farabow, Jr., Reg. No. 20,630; Arthur S. Garrett, Reg. No. 20,338; Donald R. Dunner, Reg. No. 19,073; Brian G. Brunsvold, Reg. No. 22,593; Tipton D. Jennings, IV, Reg. No. 20,645; Jerry D. Voight, Reg. No. 23,020; Laurence R. Hefter, Reg. No. 20,827; Kenneth E. Payne, Reg. No. 23,098; Herbert H. Mintz, Reg. No. 26,691; C. Larry O'Rourke, Reg. No. 26,014; Albert J. Santorelli, Reg. No. 22,610; Michael C. Elmer, Reg. No. 25,857; Richard H. Smith, Reg. No. 20,609; Stephen L. Peterson, Reg. No. 26,325; John M. Romary,**

Reg. No. 26,331; Bruce C. Zotter, Reg. No. 27,680; Dennis P. O'Reilley, Reg. No. 27,932; Allen M. Sokal, Reg. No. 26,695; Robert D. Bajefsky, Reg. No. 25,387; Richard L. Stroup, Reg. No. 28,478; David W. Hill, Reg. No. 28,220; Thomas L. Irving, Reg. No. 28,619; Charles E. Lipsey, Reg. No. 28,165; Thomas W. Winland, Reg. No. 27,605; Basil J. Lewris, Reg. No. 28,818; Martin I. Fuchs, Reg. No. 28,508; E. Robert Yoches, Reg. No. 30,120; Barry W. Graham, Reg. No. 29,924; Susan Haberman Griffen, Reg. No. 30,907; Richard B. Racine, Reg. No. 30,415; Thomas H. Jenkins, Reg. No. 30,857; Robert E. Converse, Jr., Reg. No. 27,432; Clair X. Mullen, Jr., Reg. No. 20,348; Christopher P. Foley, Reg. No. 31,354; John C. Paul, Reg. No. 30,413; Roger D. Taylor, Reg. No. 28,992; David M. Kelly, Reg. No. 30,953; Kenneth J. Meyers, Reg. No. 25,146; Carol P. Einaudi, Reg. No. 32,220; Walter Y. Boyd, Jr., Reg. No. 31,738; Steven M. Anzalone, Reg. No. 32,095; Jean B. Fordis, Reg. No. 32,984; Barbara C. McCurdy, Reg. No. 32,120; James K. Hammond, Reg. No. 31,964; Richard V. Burgujian, Reg. No. 31,744; J. Michael Jakes, Reg. No. 32,824; Dirk D. Thomas, Reg. No. 32,600; Thomas W. Banks, Reg. No. 32,719; Christopher P. Isaac, Reg. No. 32,616; Bryan C. Diner, Reg. No. 32,409; M. Paul Barker, Reg. No. 32,013; Andrew Chanho Sonu, Reg. No. 33,457; David S. Forman, Reg. No. 33,694; Vincent P. Kovalick, Reg. No. 32,867; James W. Edmondson, Reg. No. 33,871; Michael R. McGurk, Reg. No. 32,045; Joann M. Neth, Reg. No. 36,363; Gerson S. Panitch, Reg. No. 33,751; Cheri M. Taylor, Reg. No. 33,216; Charles E. Van Horn, Reg. No. 40,266; Linda A. Wadler, Reg. No. 33,218; Jeffrey A. Berkowitz, Reg. No. 36,743; Michael R. Kelly, Reg. No. 33,921;

and James B. Monroe, Reg. No. 33,971; both jointly and separately to be attorneys for American Cyanamid Company with regard to A Request for Certificate of Correction under 35 U.S.C. § 254, or in the Alternative, A Petition Under 37 C.F.R. § 1.182 to Reset the Effect of a Terminal Disclaimer in Accordance with 35 U.S.C. § 154(c)(1) of U.S. Patent 4,626,538 and to transact all business in the Patent and Trademark Office connected therewith.

The inventors originally named in the above-identified Patent No. 4,626,538 have assigned their rights to American Cyanamid Company by virtue of assignment to American Cyanamid Company recorded at Reel 4406, Frames 0769.

The undersigned, whose title appears below, is empowered to sign on behalf of the assignee in this matter.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Please send all future correspondence concerning the above matter to

Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P., at the following address:

Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P.
1300 I Street, N.W.
Washington, D.C. 20005-3315

AMERICAN CYANAMID COMPANY

Date: June 11, 1999

Egon E. Berg
Name: Egon E. Berg

Title: Assistant Secretary

EXHIBIT B

EXHIBIT C

United States Patent [19]

Dusza et al.

[11] **Patent Number: 4,521,422**

[45] **Date of Patent: Jun. 4, 1985**

[54] **ARYL AND HETEROARYL[7-(ARYL AND HETEROARYL)PYRAZOLO[1,5-a]PYRIMIDIN-3-YL]METHANONES**

[75] Inventors: **John P. Dusza**, Nanuet, N.Y.; **Andrew S. Tomcufcik**, Old Tappan, N.J.; **Jay D. Albright**, Nanuet, N.Y.

[73] Assignee: **American Cyanamid Company**, Stamford, Conn.

[21] Appl. No.: **612,812**

[22] Filed: **May 24, 1984**

Related U.S. Application Data

[63] Continuation-in-part of Ser. No. 506,966, Jun. 23, 1983, abandoned.

[51] **Int. Cl.**[3] **C07D 487/04; A61K 31/505**

[52] **U.S. Cl.** **514/258**; 544/281; 514/906

[58] **Field of Search** 544/281; 424/251

[56] **References Cited**

U.S. PATENT DOCUMENTS

4,178,449	12/1979	Dusza et al.	544/281
4,236,005	11/1980	Dusza et al.	544/281
4,281,000	7/1981	Dusza et al.	544/281

Primary Examiner—Donald G. Daus
Assistant Examiner—S. A. Gibson
Attorney, Agent, or Firm—Anne M. Rosenblum

[57] **ABSTRACT**

Aryl and heteroaryl[7-(aryl and heteroaryl)-pyrazolo[1,5-a]pyrimidin-3-yl]methanones which are new compounds active as anxiolytic, anticonvulsant, sedative-hypnotic and skeletal muscle relaxant agents in mammals and the novel process of making these compounds.

31 Claims, No Drawings

EXHIBIT D

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office

Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

SERIAL NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
06/732,986	05/13/85	DUSZA J	29,995

SUSAN H. RAUCH
1937 W. MAIN ST., P.O. BOX 60
STAMFORD, CT 06904-0060

EXAMINER	
KAPNER, S	
ART UNIT	PAPER NUMBER
122	2

DATE MAILED: ~~11/22/85~~ Feb. 22, 1986

This is a communication from the examiner in charge of your application.

COMMISSIONER OF PATENTS AND TRADEMARKS

☑ This application has been examined ☐ Responsive to communication filed on _____ ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), ____ days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☑ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449
4. ☐ Notice of Informal Patent Application, Form PTO-152
5. ☐ Information on How to Effect Drawing Changes, PTO-1474
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☑ Claims 1-19 are pending in the application.

   Of the above, claims 15-17 and 19 are withdrawn from consideration.

2. ☐ Claims _____ have been cancelled.

3. ☐ Claims _____ are allowed.

4. ☑ Claims 1-14 and 18 are rejected.

5. ☐ Claims _____ are objected to.

6. ☐ Claims _____ are subject to restriction or election requirement.

7. ☐ This application has been filed with informal drawings which are acceptable for examination purposes until such time as allowable subject matter is indicated.

8. ☐ Allowable subject matter having been indicated, formal drawings are required in response to this Office action.

9. ☐ The corrected or substitute drawings have been received on _____. These drawings are ☐ acceptable; ☐ not acceptable (see explanation).

10. ☐ The ☐ proposed drawing correction and/or the ☐ proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).

11. ☐ The proposed drawing correction, filed _____, has been ☐ approved. ☐ disapproved (see explanation). However, the Patent and Trademark Office no longer makes drawing changes. It is now applicant's responsibility to ensure that the drawings are corrected. Corrections MUST be effected in accordance with the instructions set forth on the attached letter "INFORMATION ON HOW TO EFFECT DRAWING CHANGES", PTO-1474.

12. ☐ Acknowledgment is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.

13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

14. ☐ Other

AFA 10/24/85

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-18, drawn to compounds, compositions and a method of use, classified in Class 544, subclass 281 and Class 514, subclass 258.

II. Claim 19, drawn to a process for making the compounds, classified in Class 544, subclass 281.

In the event that the invention of group I is elected, a single method of use must be chosen.

The inventions are distinct, each from the other, because of the following reasons:

Inventions I and II are related as process of making and product made.

The inventions are distinct if either (1) the process as claimed can be used to make another and materially different product, or (2) the product as claimed can be made by another and materially different process. MPEP 806.05(f).

In this case, the product as claimed can be made by a materially different process such as that described in Dugza '422.

The inventions of group I, claims 14-17 are distinct because the product may be used in four materially different processes as set forth in claims 14-17. See MPEP 806.05(h).

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject

matter, restriction for examination purposes as indicated is proper.

During a telephone conversation with Susan H. Rauch on November 6, 1985 a provisional election was made with right of traverse to prosecute the invention of group I, claims 1-14 and 18. Affirmation of this election must be made by applicant in responding to this Office action. Claims 15-17 and 19 are withdrawn from further consideration by the examiner as being drawn to a nonelected invention. See 37 CFR 1.142(b).

The method of use of claim 14 was elected.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(h).

Claims 1-14 and 18 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the prior invention as set forth in claims 1-31 of U.S. patent no. 4,521,422. Although the conflicting claims are not identical, they are not patentably distinct from each other because the distinction between the R_4 substituents claimed instantly and the R_1 groups of '422 is not deemed patentable.

RCM. 12/30/85

Claims 1-14 and 18 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-14 and 18 of copending application serial no. 732,985. Although the conflicting claims are not identical, they are not patentably distinct from each other because the differences in substituents between R_1 in 732,985 and R_4 instantly are not deemed patentably distinct.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The obviousness-type double patenting rejection is a judicially established doctrine based upon public policy and is primarily intended to prevent prolongation of monopoly by prohibiting claims in a second patent not patentably distinct from claims in a first patent. In re Vogel, 164 USPQ 619 (CCPA 1970). A timely filed terminal disclaimer in compliance with 37 CFR 1.321(b) would overcome an actual or provisional rejection on this ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78(d).

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Copies of references are not provided since they are applicants own and are therefore presumed to be easily obtainable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to S. Kapner whose telephone number is (703) 557-3979.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 557-3920.

SK
Kapner:ce
11-13-85

Mark L. Berch
Primary Examiner
Art Unit 122

KCM 12/30/85

EXHIBIT E

29,995

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

JOHN PAUL DUSZA,
ANDREW STEPHEN TONCUFCIK and
JAY DONALD ALBRIGHT

Serial No.: 732,986 Group Art Unit: 122

Filed: May 13, 1985 Examiner: S. Kapner

For: [7-(3-DISUBSTITUTED AMINO)-PHENYL]PYRAZOLO[1,5-a]-PYRIMIDINES

Commissioner of Patents
and Trademarks
Washington, D.C. 20231

S I R :

TERMINAL DISCLAIMER PURSUANT
TO 37 C.F.R. 1.321(b)

Your petitioner, AMERICAN CYANAMID COMPANY, a corporation organized and existing under the laws of the State of Maine and having its executive offices at One Cyanamid Plaza, Wayne, in the County of Passaic and State of New Jersey, represents that it is the assignee of the entire right, title and interest in application Serial No. 732,986, filed May 13, 1985, for [7-(3-DISUBSTITUTED AMINO)PHENYL]PYRAZOLO[1,5-a]PYRIMIDINES by an assignment recorded in the United States Patent and Trademark Office on May 13, 1985.

Your petitioner, AMERICAN CYANAMID COMPANY, hereby disclaims the terminal part of any patent granted on the above-identified application which would extend beyond June 3, 2002, and hereby agrees that any patent so granted on the above-identified application shall be enforceable only for and during such period that the legal title to said patent shall be the same as the legal title to United States Letters Patent No. 4,521,422 and to any patent which might issue on application Serial No. 732,985; this agreement to run with any patent granted on the above-identified application and to be binding upon the grantee, its successors or assigns.

AMERICAN CYANAMID COMPANY

By John T. Hagan
John T. Hagan, Manager
Patent Law Department

EXHIBIT F

29,995

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

JOHN PAUL DUSZA,
ANDREW STEPHEN TOMCUFCIK and
JAY DONALD ALBRIGHT

Serial No.: 732,986 Group Art Unit: 122

Filed: May 13, 1985 Examiner: S. Kapner

For: [7-(3-DISUBSTITUTED AMINO)-PHENYL]PYRAZOLO[1,5-a]-PYRIMIDINES

Stamford, Connecticut
April 21, 1986

Commissioner of Patents
and Trademarks
Washington, D.C. 20231

Sir:

AMENDMENT

In response to the Office Action mailed November 22, 1985, kindly amend the above-identified case as follows:

IN THE SPECIFICATION:

Page 1, line 3 (of CROSS REFERENCE), after "May 24, 1984," insert -- Patent No. 4,521,422, --.

Page 4, line 16, delete "of our copending application Serial No." and substitute therefor -- U.S. Patent No. 4,521,422, --; and

line 17, delete "612,812,".

IN THE CLAIMS:

Cancel Claims 15-17 and 19.

REMARKS

Applicants affirm their election to prosecute the invention of Group I, i.e., Claims 1-14 and 18. Moreover, Applicants cancel Claims 15-17 and 19. Notwithstanding cancelation of Claims 15-17 and 19, the inventorship of the Application is unchanged. Each of the originally-designated Applicants remains an inventor of the Application as amended.

Applicants have amended the Specification on pages 1 and 4 to reflect the issuance of their co-pending Application Serial No. 612,812 as U.S. Patent No. 4,521,422. These amendments do not constitute new matter.

Claims 1-14 and 18 are rejected as double patenting of the obviousness type over U.S. Patent No. 4,521,422 and provisionally rejected as double patenting of the obviousness type over their

copending Application Serial No. 732,985. To overcome these rejections, pursuant to 37 C.F.R. §1.321(b), Applicants are submitting herewith Assignee's disclaimer of the term of any patent granted on the above-identified Application which would extend beyond the expiration date of U.S. Patent No. 4,521,422 (June 3, 2002) and Assignee's acknowledgement that any patent granted on said Application would be enforceable only for such time as its legal title is identical to the legal title of U.S. Patent No. 4,521,422 and to any patent which might issue on Application Serial No. 732,985.

In view of the terminal disclaimer, Claims 1-14 and 18 are patentable over U.S. Patent No. 4,521,422 and any patent issuing on Application Serial No. 732,985.

Applicants' attorney has reviewed the references cited but not applied by the Examiner, and agrees that the instant invention is patentable thereover.

This Application now being in condition for allowance, Applicants request that the Examiner allow it to issue.

Authorization for the fee for an extension of time to reply pursuant to 37 C.F.R. §§1.136 and 1.17 to be charged to Assignee's Deposit Account is contained in the Petition submitted herewith. No additional fees are due.

Respectfully submitted,

Susan H. Rauch

Susan H. Rauch
Attorney of Record
Registration No. 31,130

AMERICAN CYANAMID COMPANY
1937 West Main Street
Stamford, Connecticut
06904-0060
(203)348-7331 ext. 2701

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner of Patents and Trademarks, Washington, D. C. 20231, on April 21, 1992
(Date of Deposit)

Susan H. Rauch
Name of Applicant, Assignee, or Registered Representative

Susan H. Rauch
Signature

April 21, 1992
Date of Signature

EXHIBIT G

"(A) while domiciled in the United States, and serving in any other country in connection with operations by or on behalf of the United States,

"(B) while domiciled in a NAFTA country and serving in another country in connection with operations by or on behalf of that NAFTA country, or

"(C) while domiciled in a WTO member country and serving in another country in connection with operations by or on behalf of that WTO member country,

that person shall be entitled to the same rights of priority in the United States with respect to such invention as if such invention had been made in the United States, that NAFTA country, or that WTO member country, as the case may be.

"(3) USE OF INFORMATION.—To the extent that any information in a NAFTA country or a WTO member country concerning knowledge, use, or other activity relevant to proving or disproving a date of invention has not been made available for use in a proceeding in the Patent and Trademark Office, a court, or any other competent authority to the same extent as such information could be made available in the United States, the Commissioner, court, or such other authority shall draw appropriate inferences, or take other action permitted by statute, rule, or regulation, in favor of the party that requested the information in the proceeding.

"(b) DEFINITIONS.—As used in this section—

"(1) the term 'NAFTA country' has the meaning given that term in section 2(4) of the North American Free Trade Agreement Implementation Act; and

"(2) the term 'WTO member country' has the meaning given that term in section 2(10) of the Uruguay Round Agreements Act.".

35 USC 104 note.

(b) EFFECTIVE DATE.—

(1) IN GENERAL.—Except as provided in paragraph (2), the amendment made by this section shall apply to all patent applications that are filed on or after the date that is 12 months after the date of entry into force of the WTO Agreement with respect to the United States.

(2) ESTABLISHMENT OF DATE.—An applicant for a patent, or a patentee, may not establish a date of invention for purposes of title 35, United States Code, that is earlier than 12 months after the date of entry into force of the WTO Agreement with respect to the United States by reference to knowledge or use, or other activity, in a WTO member country, except as provided in sections 119 and 365 of such title.

SEC. 532. PATENT TERM AND INTERNAL PRIORITY.

(a) PATENT RIGHTS.—

(1) CONTENTS AND TERM OF PATENT.—Section 154 of title 35, United States Code, is amended to read as follows:

"§ 154. Contents and term of patent

"(a) IN GENERAL.—

"(1) CONTENTS.—Every patent shall contain a short title of the invention and a grant to the patentee, his heirs or assigns, of the right to exclude others from making, using, offering for sale, or selling the invention throughout the United States or importing the invention into the United States, and,

if the invention is a process, of the right to exclude others from using, offering for sale or selling throughout the United States, or importing into the United States, products made by that process, referring to the specification for the particulars thereof.

"(2) TERM.—Subject to the payment of fees under this title, such grant shall be for a term beginning on the date on which the patent issues and ending 20 years from the date on which the application for the patent was filed in the United States or, if the application contains a specific reference to an earlier filed application or applications under section 120, 121, or 365(c) of this title, from the date on which the earliest such application was filed.

"(3) PRIORITY.—Priority under section 119, 365(a), or 365(b) of this title shall not be taken into account in determining the term of a patent.

"(4) SPECIFICATION AND DRAWING.—A copy of the specification and drawing shall be annexed to the patent and be a part of such patent.

"(b) TERM EXTENSION.—

"(1) INTERFERENCE DELAY OR SECRECY ORDERS.—If the issue of an original patent is delayed due to a proceeding under section 135(a) of this title, or because the application for patent is placed under an order pursuant to section 181 of this title, the term of the patent shall be extended for the period of delay, but in no case more than 5 years.

"(2) EXTENSION FOR APPELLATE REVIEW.—If the issue of a patent is delayed due to appellate review by the Board of Patent Appeals and Interferences or by a Federal court and the patent is issued pursuant to a decision in the review reversing an adverse determination of patentability, the term of the patent shall be extended for a period of time but in no case more than 5 years. A patent shall not be eligible for extension under this paragraph if it is subject to a terminal disclaimer due to the issue of another patent claiming subject matter that is not patentably distinct from that under appellate review.

"(3) LIMITATIONS.—The period of extension referred to in paragraph (2)—

"(A) shall include any period beginning on the date on which an appeal is filed under section 134 or 141 of this title, or on which an action is commenced under section 145 of this title, and ending on the date of a final decision in favor of the applicant;

"(B) shall be reduced by any time attributable to appellate review before the expiration of 3 years from the filing date of the application for patent; and

"(C) shall be reduced for the period of time during which the applicant for patent did not act with due diligence, as determined by the Commissioner.

"(4) LENGTH OF EXTENSION.—The total duration of all extensions of a patent under this subsection shall not exceed 5 years.

"(c) CONTINUATION.—

"(1) DETERMINATION.—The term of a patent that is in force on or that results from an application filed before the date that is 6 months after the date of the enactment of the Uruguay

Round Agreements Act shall be the greater of the 20-year term as provided in subsection (a), or 17 years from grant, subject to any terminal disclaimers.

"(2) REMEDIES.—The remedies of sections 283, 284, and 285 of this title shall not apply to Acts which—

"(A) were commenced or for which substantial investment was made before the date that is 6 months after the date of the enactment of the Uruguay Round Agreements Act; and

"(B) became infringing by reason of paragraph (1).

"(3) REMUNERATION.—The acts referred to in paragraph (2) may be continued only upon the payment of an equitable remuneration to the patentee that is determined in an action brought under chapter 28 and chapter 29 (other than those provisions excluded by paragraph (2)) of this title.".

(2) PROVISION OF FURTHER LIMITED REEXAMINATION AND CONDITIONS OF RESTRICTION REQUIREMENTS.—(A) The Commissioner of Patents and Trademarks shall prescribe regulations to provide for further limited reexamination of applications that have been pending for 2 years or longer as of the effective date of section 154(a)(2) of title 35, United States Code, as added by paragraph (1) of this subsection, taking into account any reference made in such application to any earlier filed application under section 120, 121, or 365(c) of such title. The Commissioner may establish appropriate fees for such further limited reexamination.

35 USC 154 note.
Regulations.

(B) The Commissioner of Patents and Trademarks shall prescribe regulations to provide for the examination of more than 1 independent and distinct invention in an application that has been pending for 3 years or longer as of the effective date of section 154(a)(2) of title 35, United States Code, as added by paragraph (1) of this subsection, taking into account any reference made in such application to any earlier filed application under section 120, 121, or 365(c) of such title. The Commissioner may establish appropriate fees for such examination.

(b) ESTABLISHMENT OF A DOMESTIC PRIORITY SYSTEM.—

(1) IN GENERAL.—Section 119 of title 35, United States Code, is amended—

(A) by amending the section caption to read as follows:

"§ 119. Benefit of earlier filing date; right of priority";

(B) by designating the undesignated paragraphs as subsections (a), (b), (c), and (d), respectively; and

(C) by adding at the end the following:

"(e)(1) An application for patent filed under section 111(a) or section 363 of this title for an invention disclosed in the manner provided by the first paragraph of section 112 of this title in a provisional application filed under section 111(b) of this title, by an inventor or inventors named in the provisional application, shall have the same effect, as to such invention, as though filed on the date of the provisional application filed under section 111(b) of this title, if the application for patent filed under section 111(a) or section 363 of this title is filed not later than 12 months after the date on which the provisional application was filed and if it contains or is amended to contain a specific reference to the provisional application.

"(2) A provisional application filed under section 111(b) of this title may not be relied upon in any proceeding in the Patent and Trademark Office unless the fee set forth in subparagraph (A) or (C) of section 41(a)(1) of this title has been paid and the provisional application was pending on the filing date of the application for patent under section 111(a) or section 363 of this title.".

(2) FEES.—Section 41(a)(1) of title 35, United States Code, is amended by adding at the end the following:

"(C) On filing each provisional application for an original patent, $150.".

(3) APPLICATIONS.—Section 111 of title 35, United States Code, is amended to read as follows:

"§ 111. Application

"(a) IN GENERAL.—

"(1) WRITTEN APPLICATION.—An application for patent shall be made, or authorized to be made, by the inventor, except as otherwise provided in this title, in writing to the Commissioner.

"(2) CONTENTS.—Such application shall include—

"(A) a specification as prescribed by section 112 of this title;

"(B) a drawing as prescribed by section 113 of this title; and

"(C) an oath by the applicant as prescribed by section 115 of this title.

"(3) FEE AND OATH.—The application must be accompanied by the fee required by law. The fee and oath may be submitted after the specification and any required drawing are submitted, within such period and under such conditions, including the payment of a surcharge, as may be prescribed by the Commissioner.

"(4) FAILURE TO SUBMIT.—Upon failure to submit the fee and oath within such prescribed period, the application shall be regarded as abandoned, unless it is shown to the satisfaction of the Commissioner that the delay in submitting the fee and oath was unavoidable or unintentional. The filing date of an application shall be the date on which the specification and any required drawing are received in the Patent and Trademark Office.

"(b) PROVISIONAL APPLICATION.—

"(1) AUTHORIZATION.—A provisional application for patent shall be made or authorized to be made by the inventor, except as otherwise provided in this title, in writing to the Commissioner. Such application shall include—

"(A) a specification as prescribed by the first paragraph of section 112 of this title; and

"(B) a drawing as prescribed by section 113 of this title.

"(2) CLAIM.—A claim, as required by the second through fifth paragraphs of section 112, shall not be required in a provisional application.

"(3) FEE.—(A) The application must be accompanied by the fee required by law.

"(B) The fee may be submitted after the specification and any required drawing are submitted, within such period and

under such conditions, including the payment of a surcharge, as may be prescribed by the Commissioner.

"(C) Upon failure to submit the fee within such prescribed period, the application shall be regarded as abandoned, unless it is shown to the satisfaction of the Commissioner that the delay in submitting the fee was unavoidable or unintentional.

"(4) FILING DATE.—The filing date of a provisional application shall be the date on which the specification and any required drawing are received in the Patent and Trademark Office.

"(5) ABANDONMENT.—The provisional application shall be regarded as abandoned 12 months after the filing date of such application and shall not be subject to revival thereafter.

"(6) OTHER BASIS FOR PROVISIONAL APPLICATION.—Subject to all the conditions in this subsection and section 119(e) of this title, and as prescribed by the Commissioner, an application for patent filed under subsection (a) may be treated as a provisional application for patent.

"(7) NO RIGHT OF PRIORITY OR BENEFIT OF EARLIEST FILING DATE.—A provisional application shall not be entitled to the right of priority of any other application under section 119 or 365(a) of this title or to the benefit of an earlier filing date in the United States under section 120, 121, or 365(c) of this title.

"(8) APPLICABLE PROVISIONS.—The provisions of this title relating to applications for patent shall apply to provisional applications for patent, except as otherwise provided, and except that provisional applications for patent shall not be subject to sections 115, 131, 135, and 157 of this title.".

(c) CONFORMING CHANGES.—

(1) Section 156(a)(2) of title 35, United States Code, is amended by inserting "under subsection (e)(1) of this section" after "extended".

(2) Section 172 of title 35, United States Code, is amended—

(A) by striking "section 119" and inserting "subsections (a) through (d) of section 119"; and

(B) by inserting at the end the following new sentence: "The right of priority provided for by section 119(e) of this title shall not apply to designs.".

(3) Section 173 of title 35, United States Code, is amended by inserting "from the date of grant" after "years".

(4) Section 365 of title 35, United States Code, is amended—

(A) in subsection (a), by striking "section 119" and inserting "subsections (a) through (d) of section 119"; and

(B) in subsection (b), by striking "the first paragraph of section 119" and inserting "section 119(a)".

(5) Section 373 of title 35, United States Code, is amended by striking "section 119" and inserting "subsections (a) through (d) of section 119".

(6) The table of sections for chapter 11 of title 35, United States Code, is amended—

(A) by striking the item relating to section 111 and inserting the following:

"111. Application.";

and

(B) by striking the item relating to section 119 and inserting the following:

"119. Benefit of earlier filing date; right of priority.".

SEC. 533. PATENT RIGHTS.

(a) DEFINITION OF INFRINGEMENT.—Section 271 of title 35, United States Code, is amended—

(1) in subsection (a)—

(A) by inserting ", offers to sell," after "uses"; and

(B) by inserting "or imports into the United States any patented invention" after "the United States";

(2) in subsection (c), by striking "sells" and inserting "offers to sell or sells within the United States or imports into the United States";

(3) in subsection (e)—

(A) in paragraph (1), by striking "or sell" and inserting "offer to sell, or sell within the United States or import into the United States";

(B) in paragraph (3), by striking "or selling" and inserting "offering to sell, or selling within the United States or importing into the United States";

(C) in paragraph (4)(B), by striking "or sale" and inserting "offer to sell, or sale within the United States or importation into the United States"; and

(D) in paragraph (4)(C), by striking "or sale" and inserting "offer to sell, or sale within the United States or importation into the United States";

(4) in subsection (g)—

(A) by striking "sells" and inserting "offers to sell, sells,";

(B) by striking "importation, sale," and inserting "importation, offer to sell, sale,"; and

(C) by striking "other use or" and inserting "other use, offer to sell, or"; and

(5) by adding at the end the following:

"(i) As used in this section, an 'offer for sale' or an 'offer to sell' by a person other than the patentee, or any designee of the patentee, is that in which the sale will occur before the expiration of the term of the patent.".

(b) CONFORMING AMENDMENTS.—

(1) Paragraph (2) of section 41(c) of title 35, United States Code, is amended to read as follows:

"(2) A patent, the term of which has been maintained as a result of the acceptance of a payment of a maintenance fee under this subsection, shall not abridge or affect the right of any person or that person's successors in business who made, purchased, offered to sell, or used anything protected by the patent within the United States, or imported anything protected by the patent into the United States after the 6-month grace period but prior to the acceptance of a maintenance fee under this subsection, to continue the use of, to offer for sale, or to sell to others to be used, offered for sale, or sold, the specific thing so made, purchased, offered for sale, used, or imported. The court before which such matter is in question may provide for the continued manufacture, use, offer for sale, or sale of the thing made, purchased, offered for sale, or used within the United States, or imported into the United States, as specified, or for the manufacture, use, offer for sale,

EXHIBIT H

THE URUGUAY ROUND AGREEMENTS ACT

STATEMENT OF ADMINISTRATIVE ACTION

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This Statement of Administrative Action is submitted to the Congress in compliance with section 1103 of the Omnibus Trade and Competitiveness Act of 1988 (1988 Act) and accompanies the implementing bill for the Agreement Establishing the World Trade Agreement and the agreements annexed to that Agreement (the Uruguay Round agreements). The bill approves and makes statutory changes required or appropriate to implement the Uruguay Round agreements, which the United States Trade Representative (Trade Representative) signed on April 15, 1994, on behalf of the United States under the authority of section 1102 of the 1988 Act.

This Statement describes significant administrative actions proposed to implement the Uruguay Round agreements. In addition, incorporated into this Statement are two other statements required under section 1103: (1) an explanation of how the implementing bill and proposed administrative action will change or affect existing law; and (2) a statement setting forth the reasons why the implementing bill and proposed administrative action are necessary or appropriate to carry out the Uruguay Round agreements.

As is the case with earlier Statements of Administrative Action submitted to the Congress in connection with fast-track trade bills, this Statement represents an authoritative expression by the Administration concerning its views regarding the interpretation and application of the Uruguay Round agreements, both for purposes of U.S. international obligations and domestic law. Furthermore, the Administration understands that it is the expectation of the Congress that future Administrations will observe and apply the interpretations and commitments set out in this Statement. Moreover, since this Statement will be approved by the Congress at the time it implements the Uruguay Round agreements, the interpretations of those agreements included in this Statement carry particular authority.

For ease of reference, this Statement generally follows the organization of the Uruguay Round agreements. The Statement begins with the Agreement Establishing the World Trade Organization, addresses in order each multilateral agreement contained in annexes 1 and 2 of that Agreement, and, finally, addresses the two "plurilateral" agreements that the United States will join when it enters the WTO.

In each case, the Statement first briefly summarizes the most important provisions of the particular agreement. Next, the Statement describes the pertinent provisions of the implementing bill, explaining how the bill changes or affects existing law and stating why those provisions are required or appropriate to implement the agreement. Finally, the Statement describes the administrative action proposed to implement the particular agreement, explaining how the proposed action changes existing administrative practice and stating why the changes are required or appropriate to implement the agreement.

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The Statement also addresses Title VII of the implementing bill -- the revenue provisions of the bill -- following the discussion of the two "plurilateral" agreements.

It should be noted that this Statement does not, for the most part, discuss those many instances in which U.S. law or administrative practice will remain unchanged under the Uruguay Round agreements. In many cases, U.S. laws and regulations are already in conformity with the obligations imposed by those agreements. In other cases, U.S. laws and regulations are "grandfathered" (*i.e.*, exempted) from the obligations of certain Uruguay Round agreements.

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In a few instances where there have been frequent questions from the public or the Congress, the Statement notes examples of specific statutes, regulations or practices that do *not* have to be changed as a result of the Agreement. Because this Statement is designed to describe *changes* in U.S. laws and regulations proposed to implement the Uruguay Round agreements, however, the Statement concentrates on those changes and generally does not attempt to enumerate instances in which no change in existing law or practice will be required.

Finally, references in this Statement to particular sections of U.S. statutes are based on those statutes in effect as of the date this Statement was submitted to the Congress.

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AGREEMENT ON TRADE-RELATED ASPECTS OF INTELLECTUAL PROPERTY RIGHTS

A. SUMMARY OF PROVISIONS

The Agreement on Trade-Related Aspects of Intellectual Property Rights (Agreement on TRIPs) establishes comprehensive standards for the protection of intellectual property and the enforcement of intellectual property rights in WTO member countries. It requires each WTO member country to apply the substantive obligations of the world's most important intellectual property conventions, supplements those conventions with substantial additional protection, and ensures that critical enforcement procedures will be available in each member country to safeguard intellectual property rights. The Agreement requires few changes in U.S. law and regulations and does not affect U.S. law or practice relating to parallel importation of products protected by intellectual property rights.

The Agreement is organized in seven parts. Part I deals with general principles. Part II provides standards for protection for various forms of intellectual property, copyright and neighboring rights, trademarks, geographical indications, industrial designs, patents, integrated circuit layout designs, and trade secrets. Part III regulates enforcement of intellectual property rights and Part IV deals with procedures for acquiring and maintaining such rights. Finally, the Agreement provides for dispute prevention and settlement in Part V, transitional arrangements in Part VI, and institutional and final provisions in Part VII.

1. Compliance with Multilateral Conventions

Article 2 of the Agreement requires each WTO member country to give effect to the substantive obligations of the *Paris Convention for the Protection of Industrial Property* (1967). Article 9 provides that member countries must also comply with Articles 1 through 21 and the appendix of the *Berne Convention for the Protection of Literary and Artistic Works* (1971). The United States is already a party to each of these conventions. The Agreement creates no rights or obligations with respect to authors' "moral rights" under Article 6 *bis* of the Berne Convention.

2. National Treatment and Most-Favored-Nation Treatment

Article 3 imposes a broad national treatment obligation on each WTO member country with respect to intellectual property protection. It requires each government to give "nationals" from other member countries treatment that is no less favorable than that which it gives to its own nationals with regard to the protection of intellectual property rights. The term "national" is defined by reference to the criteria for eligibility for protection under four relevant international conventions (the Paris, Berne, and Rome Conventions and the *Treaty on Intellectual Property in Respect of Protection of Integrated Circuits*). Any person or

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entity that qualifies for protection under these four conventions will be entitled to protection on a national treatment basis by all WTO member countries under the Agreement on TRIPs.

The Agreement also includes a broad most-favored-nation (MFN) obligation for each WTO member country. This provision requires each country to grant to nationals of other member countries any "advantage, favor, privilege or immunity" given to nationals of any other country with regard to the protection of intellectual property. A footnote to Article 3 makes clear that both the national treatment and MFN clauses generally confer rights with respect to all "matters affecting the availability, acquisition, scope, maintenance and enforcement of intellectual property rights as well as those matters affecting the use of intellectual property rights specifically addressed in this Agreement."

There are a few exceptions to the broad national treatment and MFN clauses. With respect to the rights of performers, producers of sound recordings, or broadcasting organizations, national treatment and MFN rights only cover the rights provided under the Agreement on TRIPs. Also, the Agreement permits member countries to continue to exercise exceptions to national treatment provided in certain international intellectual property agreements. Benefits from intellectual property agreements that enter into force prior to the WTO Agreement need not be extended on an MFN basis, nor do benefits from general agreements concerning judicial assistance or law enforcement. Finally, the procedural provisions of multilateral agreements negotiated under the auspices of the World Intellectual Property Organization, such as the Patent Cooperation Treaty, are exempt from these national treatment and MFN obligations.

3. Copyright and Related Rights

After defining the relationship between the Agreement on TRIPs and the Berne Convention, the Agreement reiterates the basic principle of copyright protection -- that protection extends only to expression and not to ideas, methods of operation, or mathematical concepts. This principle is embodied in section 102(b) of the U.S. Copyright Act (17 U.S.C. 101 *et. seq.*).

Article 10 of the Agreement confirms that all types of computer programs are "literary works" under the Berne Convention and requires each WTO country to protect them as such. It also requires copyright protection for compilations of data or other materials that are original by reason of their selection or arrangement.

Article 11 of the Agreement requires member countries to provide exclusive rental rights (the right to authorize or to prohibit commercial rental to the public of originals or copies of a work) with respect to at least computer programs and cinematographic works. WTO countries need not provide rental rights in respect of cinematographic works unless rental has led to widespread copying having a materially detrimental effect on the author's exclusive right of reproduction of the work.

Article 12 of the Agreement provides minimum standards for the term of protection or copyrighted works. The term of protection for many works is the life of the author plus 50 years, but whenever the term of protection is not linked to the life of a person, Article 12 requires that the term be a minimum of fifty years (except for works of applied art or photographs).

Article 9:2 of the Berne Convention now bans the imposition of limitations on, or exceptions to, the reproduction right except when such limits or exceptions do not conflict with a normal exploitation of the work and do not unreasonably prejudice the legitimate interests of the right holder. Article 13 of the Agreement on TRIPs widens the scope of this provision to all exclusive rights in copyright and related rights, thus narrowly circumscribing the limitations and exceptions that WTO member countries may impose. This approach is consistent with section 107 of Copyright Act (17 U.S.C. 107) relating to fair use of copyrighted works.

Article 14 requires member countries to provide sound recording producers a fifty-year term of protection and the right to authorize or prohibit the direct or indirect reproduction and commercial rental of their sound recordings. However, a WTO member country that on April 15, 1994, had a system of payment of equitable remuneration to compensate for rental of recordings is permitted to keep that system (only Japan and Switzerland qualify under this exception).

With respect to performers, the Agreement requires WTO countries to make it possible for performers to prevent unauthorized fixation, broadcast or reproduction of their live performances. Broadcasting organizations are to be accorded similar rights, although member countries have the option of providing protection consistent with the Rome

Convention or providing owners of copyright in works broadcasted the right to prevent the same acts. The Agreement also makes Article 18 of the Berne Convention regarding the protection of existing works explicitly applicable to sound recordings.

4. Trademarks

Article 16 of the Agreement on TRIPs sets out certain basic rights that member countries must grant to the holders of a "trademark," as defined in paragraph one of Article 15. For example, the use of identical marks on identical goods and services will be presumed to create a likelihood of confusion and thus to be improper. Additionally, Article 16 requires each member country to apply the provisions of Article 6 *bis* of the Paris Convention, concerning the protection of well-known trademarks, to service marks. This Article also clarifies the standard for determining whether a trademark is "well-known."

Article 18 of the Agreement requires that the initial registration of a trademark must be for a term of not less than seven years and that the registration of a trademark must be renewable indefinitely.

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Article 19 applies when a member country requires use of a trademark to maintain its registration. It provides that a trademark can be canceled for non-use only after an uninterrupted period of at least three years of non-use. However, countries must permit a trademark owner to establish the existence of circumstances beyond his control which led to the non-use of the trademark. Valid reasons for non-use, as set forth in Article 19, include import restrictions on or other government requirements for goods or services protected by the trademark. Use of a trademark by another person is recognized as use of the trademark for the purpose of maintaining a registration, if such use is controlled by the trademark owner.

Article 20 safeguards the role of a trademark as an indication of the source of the trademarked product or service by prohibiting imposition of special requirements, such as use with another trademark, that could impair this role. Member countries may, however, require the firm or person producing the goods or services to include its trademark along with, but not linked to, the trademark distinguishing the goods or services at issue.

5. Geographical Indications

Articles 22 through 24 provide for the protection of geographical indications for goods. Article 22 requires member countries to provide interested parties a means to prevent the use of product descriptions that mislead the public regarding the geographic origin of a good or that constitute "an act of unfair competition" under Article 10 *bis* of the Paris Convention. In addition, member countries must either refuse or invalidate the registration of a trademark that contains a false indication of geographic origin of the product that misleads the public. This Article also prohibits the use of a geographical indication which, although correctly reflecting the origin of the good, nonetheless falsely represents to the public that the good originates in another geographic location.

Article 23 provides additional protection for geographical indications for wines and spirits. A geographical indication for wines or spirits which does not originate in the location indicated may not be used or registered even though the true geographical origin is indicated on the product. "Homonymous geographical indications" remain protected to the extent that they do not falsely represent to the public that a good originates in another geographic location.

Article 24 specifies limited exceptions to Articles 22 and 23. First, if a trademark, which contains a geographical indication identifying wines or spirits, was used in a continuous manner with regard to the same or related goods or services for ten years before April 15, 1994, or in good faith before that date, the prohibition set forth in Article 23 is inapplicable. Secondly, a member country does not have to prevent continued and similar use of a geographical indication used on or in connection with goods or services that was

applied for or registered in good faith, or where rights have been acquired through good faith use, before the application of these provisions in that member country, or before the geographical indication is protected in its country of origin. These two provisions permit

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flexibility in expanding product lines covered by the affected trademark without jeopardizing rights in the trademark. Lastly, member countries may continue to use pre-existing grape varietal names for products of the vine, regardless of whether such names are geographical indications of another member country, provided that as of the date the WTO Agreement enters into force, the grape variety in question existed in the country permitting continued use. The principle underlying this provision also applies to the use of a person's own name or the name of his predecessor in business, except where the name is used in such a manner as to mislead the public.

Articles 23 and 24 provide for further negotiations on this subject. The Council on TRIPs, established under Article IV of the WTO Agreement, will oversee negotiations on a multilateral system of notification and registration of geographical indications for wines. Member countries will also negotiate on increased protection for individual geographical indications for wines and spirits. In these negotiations, the United States will seek improved protection for names of U.S. spirits that meet the definition of a geographical indication.

6. Industrial Designs

Articles 25 and 26 of the Agreement require each member country to provide protection for independently created industrial designs that are new or original and that meet the other conditions specified. Designs that are functional may be excluded from protection. The owner of a protected design must be given the right to prevent others from making or selling, for a commercial purpose, articles that copy or substantially copy the protected design. In addition, each government must provide a term of protection of at least ten years. Article 25 explicitly requires governments to provide protection for textile designs, either under an industrial design law or through copyright, to ensure that right owners can obtain protection without delay and unreasonable cost. Protection currently available under U.S. patent and copyright law meets the requirements of these articles.

7. Patents

a. Scope of Patentable Technology

Article 27 requires each WTO country to make patents available for inventions in all fields of technology, provided that the inventions are new, involve an inventive step (*i.e.*, are not obvious) and are capable of industrial application (*i.e.*, are useful). Governments will no longer be able to discriminate in respect to the enjoyment of patent rights based on the area of technology, place of invention, or whether the product is imported or locally made. Member countries may exclude particular inventions from patentability only in a few, narrowly defined cases.

WTO countries must make patent protection available for essentially all fields of technology, including pharmaceuticals, micro-organisms, and non-biological and microbiological processes. While they may deny patent protection for plants, they must

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provide for the protection of plant varieties either by patents or by an effective *sui generis* system or a combination of these two forms of protection. The United States provides both patent protection and plant breeder's rights. Those member countries that choose to implement a *sui generis* system of protection for plant varieties may adopt a system consistent with the *International Convention for the Protection of New Varieties of Plants* (UPOV Convention). The Agreement on TRIPs calls for the level of protection provided to plants and animals to be reviewed four years after the date of entry into force of the WTO Agreement. At that time, the United States will seek improved patent protection for plants and animals.

Special provisions apply to WTO member countries that do not already provide product patent protection for pharmaceutical and agricultural chemical products on the date the WTO Agreement enters into force. Each such country must immediately provide an interim system that permits patent applications for these products to be filed. When the application is examined, novelty will be determined as of the date of that filing. If a product is the subject of an application under this interim system, the country in question must provide exclusive marketing rights for a period of five years after the product receives marketing approval, or until a patent is granted or rejected, whichever period is shorter. To qualify for market exclusivity, the product must also be patented in another WTO member country and approved for marketing there.

b. Scope of Patent Rights

Article 28 specifies that a patent must include the right to exclude others from making, using, offering for sale, selling, or importing the product. The Agreement permits limited exceptions to the exclusive rights conferred by a patent if certain conditions are met. United States law contains some such exceptions, such as those set out in section 271(e) of the Patent Act (35 U.S.C. 271(e)).

The Agreement on TRIPs puts stringent conditions on use of a patented invention without the authorization of the right holder. This includes situations involving use of the invention by the government or use by a third party authorized by the government under a "compulsory" license. These conditions, including special conditions applicable to semiconductor technology, will also apply to compulsory licensing of rights protecting integrated circuit layout designs. Many foreign countries will be required to eliminate provisions that now subject patents to compulsory licenses if the patented invention is not produced locally.

c. Term of Protection

Article 33 requires that the term of protection available for a patent must be at least 20 years from the filing of the application. This provision permits member countries to provide for extensions of patent terms to yield patent terms that extend beyond twenty years measured from the filing date.

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d. Burden of Proof

A final provision in the Agreement's patent section addresses the allocation of the burden of proof with regard to enforcement of patents covering processes. The provision requires each member country to provide its judicial authorities with the power to order a party accused of infringing a patented process to prove that its product, if identical to the product that would stem from exercise of a patented process, was produced using a different process. The provision should facilitate the ability of a process patent holder to establish infringement.

8. Protection for Integrated Circuit Layout Designs

Articles 35 through 38 of the Agreement provide for the protection of semiconductor integrated circuit layout designs at a level fully consistent with the U.S. Semiconductor Chip Protection Act (17 U.S.C. 901, *et seq.*). They include provisions for the protection of a product incorporating a protected layout design and require innocent infringers to pay a reasonable royalty for the sell-off of stock on hand or on order when they receive notice that they are dealing with infringing designs. Article 37 makes the limitations on compulsory licenses in Article 31 applicable to layout designs. These conditions permit compulsory licensing of semiconductor technology only for public non–commercial use or to remedy an anti–competitive practice. Article 38 provides for a minimum ten-year term of protection.

9. Protection of Undisclosed Information

Article 39 requires each member country to provide protection to the holders of undisclosed information (trade secrets) provided the information is secret, has commercial value, and has been subject to reasonable steps to keep it secret. The Agreement lists some acts that constitute misappropriation of a trade secret and provides that acquisition of undisclosed information by a third party would in some cases constitute misappropriation.

Article 39 also requires member countries to protect against unfair commercial use of the information they require companies to submit to obtain marketing approval of chemical or pharmaceutical products that utilize new chemical compounds.

10. Control of Anti-Competitive Practices in Contractual Licenses

Article 40 permits member countries to adopt appropriate measures to prevent or control licensing practices or conditions that may in particular cases constitute an abuse of intellectual property rights having an adverse effect on competition in the relevant market. The Article also authorizes consultations regarding allegations of anticompetitive activity in particular cases.

11. Enforcement Procedures

Part III of the Agreement establishes extensive requirements to ensure that intellectual property rights will be effectively enforced both at and inside each member country's borders. Section 1 requires each government to provide fair and transparent enforcement procedures, including by providing intellectual property right holders access to effective judicial procedures for the enforcement of intellectual property rights. If a country provides for administrative enforcement proceedings that result in a civil remedy, Article 49 requires that those procedures conform to principles equivalent in substance to the rules set out in Section 2 for judicial procedures.

Section 2, concerning judicial procedures, requires each member country to provide for preliminary and final injunctive relief, measures to preserve evidence, civil damages, and other remedies in intellectual property enforcement proceedings. The Section also includes safeguards to protect parties from abuse of litigation procedures.

Section 3 requires member countries to establish effective procedures allowing trademark and copyright owners to obtain seizures of counterfeit and pirated goods at the border, subject to certain safeguards. For example, to protect legitimate importers, Article 55 provides that actions concerning whether goods detained at the border are infringing must be initiated within ten working days in most cases and 20 working days in appropriate cases. Such actions may be initiated by the customs authorities or any party other than the defendant in the action. Bonding requirements and improved availability of information on customs actions are important elements of this section.

Section 4 permits member countries to establish border enforcement procedures for rights other than trademark and copyright, subject to certain additional safeguards. For example, if a member country implements the border enforcement provisions of the Agreement with respect to patents, integrated circuits, trade secrets, or industrial designs, any allegedly infringing products being detained by customs authorities must be released upon payment of a bond after a specified period of time. The Section also permits customs officials to take action on their own initiative to prevent the importation of infringing goods.

Under Section 5, WTO member governments must provide criminal sanctions to address willful copyright piracy and trademark counterfeiting on a commercial scale. Criminal sanctions may also be provided to address infringement of other intellectual property rights, particularly when the infringement is willful and done on a commercial scale.

12. Acquisition and Maintenance of Intellectual Property Rights and Related Inter-Partes Procedures

Article 62 permits member countries to require compliance with reasonable procedures and formalities as a condition of acquiring or maintaining rights in patents,

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trademarks, industrial designs, geographical indications, and semiconductor mask works. With respect to intellectual property rights that are subject to registration, such as patents and trademarks, member countries must ensure that their procedures permit the grant of the right within a reasonable period of time. This rule is meant to avoid unwarranted curtailment of the term of protection. Finally, governments must provide for judicial review of final administrative decisions regarding the grant of intellectual property rights, with some minor exceptions.

13. Transparency and Dispute Settlement

Article 63 requires member countries to publish, or at least make publicly available in a national language, all laws, regulations, final judicial decisions, and administrative rulings of general application that pertain to the availability, scope, acquisition, enforcement, or prevention of the abuse of intellectual property rights. They must also publish any agreements they enter into with other WTO governments.

Article 64 makes clear that disputes arising under the Agreement on TRIPs are to be settled under the terms of the WTO Dispute Settlement Understanding. However, governments may not initiate cases against other WTO countries alleging "non-violation," nullification, or impairment of benefits under the Agreement during the first five years after the WTO Agreement goes into effect. During the five-year period, the TRIPs Council may make recommendations to the WTO Ministerial Conference concerning the appropriate scope and procedures for addressing such complaints. Approval of the recommendations or any decision to extend the five-year moratorium on bringing such cases must be made by consensus.

14. Transitional Arrangements

Articles 65 and 66 define when member countries have to meet the obligations of the Agreement on TRIPs. All member countries are given a "grace period" of one year after the entry into force of the WTO Agreement before having to apply any provisions of the Agreement on TRIPs. Any developing country, and some countries that are in the process of changing from centrally-planned to market economies, must implement the national treatment and MFN provisions after the one-year grace period but may delay implementation of all other substantive TRIPs provisions for four years after that date. An additional five-year period is available for developing countries to extend product patent protection to technologies that were not formerly eligible for protection. Least-developed country members must apply the national treatment and MFN provisions after the general one-year grace period but may delay implementation of all other TRIPs provisions for ten years from that date. The TRIPs Council may grant such countries further extensions under certain circumstances. Use of any of the transitional provisions is subject to a standstill requirement, *i.e.*, any changes made during the relevant transition period cannot result in a lesser degree of consistency with the Agreement.

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15. Institutional Arrangements and Final Provisions

Article IV of the WTO Agreement establishes a Council for TRIPs to oversee the functioning of the Agreement on TRIPs. The Agreement on TRIPs provides that the Council will monitor the operation of the Agreement including compliance matters. Article 69 provides for cooperation to eliminate trade in goods that infringe intellectual property rights, for the establishment of contact points, and for information exchanges and customs cooperation in regard to trade in counterfeit trademark and pirated copyright goods.

The TRIPs Council will review the implementation of the Agreement five years after the WTO Agreement enters into force and every two years thereafter. The Council may recommend, by consensus, that the WTO Ministerial Conference amend the Agreement to adjust to higher levels of protection of intellectual property rights already in force among all member countries.

The "final provisions" on application of the Agreement provide that no member country will have any obligations in regard to acts that occurred before that country had to apply the Agreement, but the government will be bound in respect of all subject matter existing on that date. Member countries are not required to restore protection to subject-matter that has fallen into the public domain. A reservations clause bars any reservations to the Agreement unless all other member countries consent. Finally, a general security exceptions clause permits a member country to withhold information or take action for national security reasons, or to comply with obligations under the United Nations Charter for the maintenance of international peace and security.

B. ACTION REQUIRED OR APPROPRIATE TO IMPLEMENT THE AGREEMENT

1. Implementing Bill

Title V of the implementing bill makes changes in federal law with respect to:

- rental rights in computer programs;
- protection against the unauthorized fixation in a sound recording or music video of a live performance or the communication to the public of the sounds of a live performance;
- restoration of copyright protection to works already in existence and not protected by federal copyright in the United States, but that are subject to neighboring rights or copyright protection in the WTO member country that is the source of the work;

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- the definition of "abandonment" under the trademark law;
- registrability under the trademark law of a misleading geographic indication identifying wines or spirits;
- treatment of inventive activity occurring in WTO member countries for purposes of establishing the date of invention under U.S. patent law;
- the definition of infringing activity under a patent relating to offers for sale and importation of a patented good;
- the term of protection of a patent; and
- establishment of a provisional patent application system and a right of internal priority for patent applications filed originally in the United States, as well as enabling a patent applicant to extend the term of patents that are delayed by interference proceedings, secrecy orders, and successful appeals to the Board of Patent Appeals or Interferences or a federal court.

Other areas of U.S. intellectual property law are unaffected by the Agreement on TRIPs. For example, the Agreement does not require any change in current U.S. law or practice with respect to parallel importation of goods that are the subject of intellectual property rights.

ADMINISTRATIVE ACTION STATEMENT

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a. Rental Rights in Computer Programs

Article 11 of the Agreement requires member countries to provide exclusive "rental rights" (the right for authors or their successors in title to authorize or prohibit commercial rental to the public of originals or copies of their copyrighted works) in respect of at least computer programs and cinematographic works. Federal law provides rental rights for computer programs but those rights currently are subject to a "sunset" provision in the Computer Software Rental Amendments Act of 1990 (17 U.S.C. 109 note). Section 511 of the implementing bill eliminates the sunset provision so that authors of computer programs and their successors in title will enjoy rental rights on a permanent basis.

Article 11 also provides that member countries need not provide rental rights in respect of cinematographic works unless rental has led to widespread copying that is having a material effect on the author's exclusive right of reproduction of the work. Because the rental of motion pictures has not caused a widespread problem of copying in the United States, the bill does not provide for rental rights in respect of motion pictures.

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b. Bootleg Sound Recordings and Music Videos

Article 14 of the Agreement requires WTO members to make it possible for performers to prevent the unauthorized fixation in a sound recording of their performances and to prevent the reproduction of such recordings. Various state statutes and judicial decisions presently provide criminal sanctions and civil remedies for "bootleg" recordings or reproduction of such recordings. However, these laws and decisions are not entirely uniform and may not provide the necessary basis for border enforcement against bootleg sound recordings. Sections 512 and 513 of the bill implement Article 14 of the Agreement by creating new federal civil and criminal remedies against bootlegging. These remedies will supplement, rather than preempt, state laws and judicial decisions on this subject.

Section 512 amends Title 17 of the U.S. Code to provide that bootleggers are subject to civil remedies under the Copyright Act. In addition, section 513 makes bootlegging "knowingly and for purposes of commercial advantage or private gain" a crime. It is intended that neither civil nor criminal liability will arise in cases where First Amendment principles are implicated, such as where small portions of an unauthorized fixation are used without permission in a news broadcast or for other purposes of comment or criticism.

The United States has led efforts to combat the rise in piracy of sound recordings in countries around the world. The new federal remedies will ensure that performers enjoy a high and uniform level of protection in the United States as well, and will aid efforts by the Customs Service to combat bootleg sound recordings.

c. Restoration of Copyright

Article 9 of the Agreement requires WTO countries to comply with the requirements of Article 18 of the *Berne Convention for the Protection of Literary and Artistic Works* (1971). In addition, Article 14 of the Agreement explicitly extends this requirement to sound recordings. Before the United States adhered to the Berne Convention in 1989, Congress determined that the United States was in compliance with Article 18 of the Convention but called for further study concerning whether to restore copyright protection to works from Berne Union member countries that had fallen into the public domain in the United States.

Since 1989, Congress, the Administration, the private sector, and the academic community have debated various approaches to restoring copyright protection to certain works in the public domain. The North American Free Trade Agreement Implementation Act (Pub. L. Law 103–182) took a first step by adding a new section 104A to the Copyright Act, which authorized the restoration of copyright protection to certain Mexican and Canadian motion pictures and works included in those films.

Section 514 of the implementing bill replaces the current version of section 104A and restores protection to virtually all copyrighted works, including sound recordings, from members of the WTO or the Berne Union that are not in the public domain in their source country through the expiration of term but are not protected under copyright law in the United States. Section 514 also provides for restoring copyright to works from countries that are not WTO or Berne Union members if they provide reciprocal treatment for U.S. works. The Administration will work to ensure that other countries provide protection for U.S. works, including sound recordings, that are not in the U.S. public domain through the expiration of their term in the United States, but are in the public domain in such countries.

Section 514 provides protection to works from eligible countries if the works are not protected by copyright in the United States because:

- the copyright owner failed to comply with one or more of the formalities required by U.S. copyright law, for instance by publishing the work without a proper copyright notice, failing to renew the copyright, or by failing to comply with the manufacturing clause or *ad interim* provisions of the copyright law;
- the work is a sound recording fixed prior to February 15, 1972, and was not entitled to copyright protection; or
- the work is from a country with which the United States did not have copyright relations at the time of the work's publication.

The bill uses the term "restoration" without distinguishing between those copyrights actually "restored" by the bill and those that have never before enjoyed copyright protection in the United States. Protection is provided in both cases.

In general, copyright will be restored on the date when the TRIPs Agreement's obligations take effect for the United States, which means that the owners of restored copyrights may seek remedies against any infringements occurring on or after that date. However, section 514 includes special provisions that will apply when a "reliance party" in the United States has commenced and continued to engage in exploitation of a restored work or has acquired one or more copies or phonorecords of a restored work. The term "reliance party" also includes a person who is a successor, assignee, or licensee of another reliance party who has sold or otherwise disposed of a derivative work based upon a restored work. It further includes a person who has acquired "significant assets" of a predecessor reliance party. Reliance parties will have a 12-month grace period, after filing of constructive or receipt of actual notice that has been served by a copyright owner to enforce the restored copyright, during which the reliance party may exploit the work in any manner except for reproduction.

(1) Copyright Restoration

Under subsection (a) of amended section 104A, copyrights in restored works will arise automatically on the date of restoration as defined in subsection (h)(2) of amended section 104A. No special steps other than those set out elsewhere in Title 17 will need to be taken to make a restored copyright fully enforceable against parties other than "reliance parties." Owners of restored copyrights will also be permitted to file for registration of the copyright simultaneously with the filing of a notice of intent to enforce a restored copyright. The notice and other formal requirements in subsections (c) through (e) of amended section 104A will apply *only* when restored copyrights are being enforced against "reliance parties."

Restored copyrights will last for the term that they would have enjoyed had they arisen and remained in force under the Copyright Act. Thus, for example:

- a French short story that was first published without copyright notice in 1935 will be treated as if it had both been published with a proper notice and properly renewed, meaning that its restored copyright will expire on December 31, 2010 (75 years after the U.S. copyright would have come into existence);

- a Chinese play from 1983 will be protected until December 31st of the fiftieth year after the year in which its author dies; or

- a Mexican sound recording first published in Mexico in 1965 will be protected until December 31, 2040.

This provision is intended to deal only with duration and does not encompass reversion or termination rights under chapters 2 and 3 of the Copyright Act.

Motion pictures and certain works included in motion pictures produced in Mexico and Canada for which copyrights were restored under the NAFTA Implementation Act will continue to enjoy copyright protection, but such protection will be governed by the new section 104A substituted by the implementing bill. Similarly, other works from NAFTA countries that are in the public domain in the United States, including motion pictures for which no NAFTA restoration was sought, will be subject to copyright restoration under the new section 104A.

(2) Ownership of a Restored Copyright

Subsection (b) of amended section 104A provides that a restored copyright is owned, in the first instance, by its author or initial right holder, as determined by the law of the restored work's "source country." This means that in certain instances it will be necessary to refer to foreign law to identify the initial owner of the restored copyright. There can be only one source country for any particular work. In the case of sound recordings, compilations, and other fixations that are "works" under U.S. law, but are

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protected by "neighboring rights" under some foreign laws, subsection (b) grants rights to the initial beneficiary of such "neighboring rights" regimes.

If the author or initial right holder at any time assigned, licensed, or otherwise alienated or disposed of an exclusive or non-exclusive interest in the copyright, that disposition is to be given effect according to the terms of the agreement, taking into account the expectations of the parties and relevant laws (including those concerning copyright, neighboring rights, contracts, descent and distribution, estates, and conflicts of law). For example, a U.S. company may have obtained rights in an underlying literary or musical work for exploitation in a motion picture "throughout the world" at a time when the underlying work was in the public domain in the United States but protected in the source country. Such a transfer would be given effect in the United States, depending on the terms of the contract as a whole.

(3) Enforcement Against "Reliance Parties"

Subsection (c) of amended section 104A provides that any owner of any exclusive interest in a restored copyright may file in the Copyright Office or serve on a reliance party a notice of intent to enforce that copyright against "reliance parties." It also makes clear that no statement or claim made in any such notice will enjoy any presumption as to its truthfulness. This provision is intended to avoid any implication that "reliance parties" (or others) face an augmented burden in contesting claims made in such notices.

The concept of "reliance party" is intended to grant, for a limited time, to persons having acted in good faith reliance on the public domain status of the now-restored work, the ability to exploit such works in most manners. It applies to two classes of persons: (1) those who acted in a certain manner prior to the date of enactment of the bill

(or, for restored works from source countries not in the Berne Union or WTO until after the WTO Agreement becomes effective with respect to the United States, the date of adherence or proclamation) and (2) those who bought or otherwise acquired an interest in restored works (or derivative works created before the date of enactment that are based on a restored work) from someone having the status of a reliance party. The first class consists of persons who either (a) engaged in acts with respect to a particular restored work, prior to the date of enactment of the Uruguay Round Agreements Act, that would have been infringing had it been copyrighted at the time (i.e., acts such as reproduction, public performance, or creation of a derivative work) *and* continued such acts after restoration, or (b) made or acquired one or more copies of a particular restored work prior to the date of enactment. Acquisition of works incorporating a material portion of a restored work are also encompassed by this provision.

The other class comprises persons who at any time either (a) bought or otherwise acquired an interest in a derivative work based upon a restored work from someone having the status of reliance party with respect to such derivative work or (b)

bought or otherwise acquired "significant assets" -- including multiple copyrights, or a back list, imprints, or tangible inventory -- from someone having the status of a reliance party.

While sometimes not technically a "reliance party," immunity from liability on like grounds is intended to be available to related parties who might otherwise be liable under doctrines such as *respondeat superior*, contributory infringement or vicarious liability, including, but not limited to, parent organizations, subsidiaries, officers, directors, shareholders, employees, agents and the like.

(4) Remedies

Subsection (d)(1) of amended section 104A provides that persons other than "reliance parties" accused of infringing restored copyrights are subject -- beginning on the date of restoration -- to full liability for acts occurring on and after that date. A restored copyright is meant to be indistinguishable from any other copyright and the holder of a restored copyright is to have exactly the same rights and remedies as any other copyright holder, except in respect to "reliance parties."

Pursuant to subsection (d)(2) of amended section 104A, no remedy may be invoked against a "reliance party" until:

- the Copyright Office has published in the Federal Register a list identifying the particular restored copyright, or
- the owner of the restored copyright serves actual notice upon the "reliance party."

Notice filed with the Copyright Office will be effective against any "reliance party," whereas actual notice will be effective with respect to the specific reliance party notified, and other reliance parties who know both of the fact of service and the contents of the notice. The Copyright Office will publish regulations that govern the filing of such notices, no later than 90 days before the TRIPs Agreement takes effect for the United States.

Any actual notice must, at a minimum, comply with the applicable provisions of subsection (e)(2) of amended section 104A, discussed below, and must be served -- whether in person or by mail -- in a manner that comports with due process. That is, "the means employed must be such as one desirous of actually informing the party might reasonably adopt to accomplish it." *Mullane v. Central Hanover Bank & Trust Co.*, 339 U.S. 306, 315 (1950). The contents of actual and constructive notices will differ in important respects because subsection (e) requires that actual notice identify the particular use to which the owner of the restored copyright objects and the work in which the restored work is used.

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The "reliance party" must cease reproducing a work in which a restored copyright subsists, and cease preparing new derivative works that reproduce significant elements of a work in which a restored copyright subsists, on the date the Copyright Office publishes the title or description of the work in the *Federal Register* or the "reliance party" receives actual notice. For 12 months thereafter, however, a "reliance party" may sell off previously manufactured stock, publicly perform or publicly display the work, or authorize others to conduct these activities. The grace period will also provide an opportunity for the parties to reach a licensing agreement to permit continued use of the work. In the absence of an agreement, the reliance party must cease using the work at the end of the grace period.

Subsection (d)(3) of amended section 104A sets out additional provisions that apply to the continued exploitation, by reliance parties, of derivative works based upon restored works, where the derivative work was created prior to the date of enactment of the bill (or, for restored works from source countries not in the Berne Union or WTO until after the WTO Agreement becomes effective with respect to the United States, the date of adherence or proclamation). Such a derivative work may continue to be exploited by a relevant reliance party if the reliance party pays the owner of the restored copyright reasonable compensation. Such compensation is due in respect of any infringing conduct for which the reliance party would be liable in the absence of the provisions of subsection (d)(3).

Although it is likely that the owner of the restored copyright and the reliance party will agree on the amount of compensation to be paid, should they fail to do so, the amount of compensation would be determined by an action in federal district court, or if the parties agree, through mediation, or binding arbitration. A judge, arbitrator or mediator should set such compensation to reflect, among other things, (a) harm to the actual or potential market for or value of the restored work and (b) the relative contributions of expression of the authors of the restored work and the derivative work. In some cases, the harm to the actual or potential market of the restored work will exceed the revenue generated by the exploitation of the derivative work. Subsection (d)(3) is not intended to limit compensation due to the owner of a restored copyright in such cases.

Section 412 of the Copyright Act generally restricts the award of statutory damages and attorney's fees to copyright holders who registered their copyrights before the infringement began. Under subsection (d)(4) of amended section 104A, in the case of reliance parties, infringement will be deemed to have commenced prior to registration, so that statutory damages and attorney's fees will not be available, when activities that would have been infringing prior to the date of restoration had the restored work then been subject to copyright, were commenced prior to the date of restoration.

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Remedies are available against "reliance parties" when the owner of the restored copyright has either filed constructive notice or served actual notice under subsection (d)(2) of amended section 104A. In considering whether an injunction should issue in respect of an infringement of a restored copyright, it is expected that a court would apply all of the traditional canons of equity. See *Campbell v. Acuff-Rose Music*, 114 S.Ct. 1164, 1171 n.10 (1994).

(5) Notices of Intent

Subsection (e) of amended section 104A establishes rules concerning notices of intent to enforce a restored copyright against reliance parties. First, in order to permit clear identification of the work subject to restored copyright and the owner of that right, subsection (e) specifies the minimum information that must be included in such a notice. All notices must identify the title of the restorable work in a manner that minimizes uncertainty as to the identity of the copyright that is intended to be enforced. Thus, an owner must provide English translations of foreign-language titles and alternative titles by which the work might be known of which the owner is aware. For a work, such as a photograph, that is unlikely to be known by any title it might have, the owner must describe the work to the extent necessary for its identification.

In addition, the notice must be signed by the owner of the restored copyright or his agent. An agent's signature is effective only if the owner has created the agency in writing prior to the time the agent signs the notice. Actual notice served on a "reliance party" must identify the allegedly infringing use but no such requirement exists for constructive notice filed with the Copyright Office.

The filing of a notice of intent to enforce a restored copyright shall not prejudice the ability of a person to seek at any time a judicial determination that a particular work was never in the public domain in the United States.

Subsection (e)(1) specifies certain information that must be included in constructive notices and also requires the Copyright Office to publish lists of restored copyrights that have been the subject of filings in the Copyright Office. The lists will be published quarterly and cumulated on an annual basis for two years after the relevant date of restoration for a particular country. The Administration expects that the initial 24-month period will be the relevant date of restoration for most countries, since more than 100 countries are Members of the Berne Union and many countries will be original members of the WTO when that Agreement enters into force. For countries that become "eligible countries" through adherence or proclamation, there will be a separate 24-month period for filing notices under subsection (e)(1) and the Copyright Office will publish lists of notices as specified above. The Copyright Office will keep at least one complete list of all notices published in its Public Information Office.

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Subsection (e)(3) provides that a notice will be void as to a particular restored work if it contains any knowingly false statements or claims with respect to that work. Thus, any notice listing multiple titles, one or more of which the purported owner does not in fact own or for which the copyright has not been restored, will be void in respect of such work and "reliance parties" may continue all uses until a proper notice is made.

(6) Immunity from Liability

Subsection (f)(1) of amended section 104A provides that when a party has warranted that a work containing (or based on) a restorable work does not infringe a copyright, and the warranty was made prior to January 1, 1995, that party will not be liable for breach of warranty when the breach is due solely to later restoration of the copyright. Subsection (f)(2) provides that neither the remedy of specific performance nor damages shall be available for a reliance party's failure to perform an obligation undertaken before January 1, 1995 when such performance has become infringing by virtue of restoration of a copyright under this Act.

(7) Other Provisions

Subsection (g) of amended 104A permits the President to proclaim a foreign country that is neither a member of the WTO nor of the Berne Union an "eligible country" for purposes of section 104A when that country makes restoration of copyrights available to U.S. works on substantially the same basis as that provided in the United States.

(8) Amendment to Section 109(a)

Section 514 also amends section 109(a) of the Copyright Act by adding a provision clarifying that the sale or other disposition of copies or phonorecords manufactured before the date a copyright is restored under amended section 104A, or in the case of a reliance party before publication or service of notice under 104A(e), will be authorized for purposes of direct or indirect commercial advantage only during the 12-month post-restoration grace period provided in section 104A(d).

d. Definition of "Abandonment" under the Trademark Act

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Under the current version of the Trademark Act of 1946, a mark is considered "abandoned" when its use has been discontinued with intent not to resume use. Furthermore, under the Trademark Act, non-use for two consecutive years is *prima facie* evidence of abandonment. Article 19.1 of the Agreement on TRIPs provides that a registration may be canceled only after three years of non-use. Accordingly, section 521 of the implementing bill amends section 45 of the Trademark Act to provide that three consecutive years of non-use will constitute *prima facie* evidence of abandonment. Section 521 makes no change in the provision in current law that permits a party to prove abandonment based on non-use (with intent not to resume use) during a shorter period of time.

e. Misleading Geographical Indications

Article 23.2 of the Agreement requires WTO member countries to refuse registration of any trademark consisting of a geographic indication misleadingly identifying wines or spirits or to invalidate any existing such trademark. Section 522 of the implementing bill amends section 2 of the Trademark Act of 1946 to provide that trademarks that consist of, or comprise, a geographical indication for wines or spirits that do not in fact originate in that geographic area will be refused registration if the mark was first used after the WTO Agreement has been in effect for one year. Any trademark containing a geographic indication that is currently registered or in use, or that is registered or in use during the period before the WTO Agreement has been in effect for a year, may be maintained.

As amended, section 2 of the Trademark Act will prohibit the registration of marks which contain a geographical indication which refers to a place other than where a good actually originates. "Geographical indications" are defined in TRIPs Article 22.1 as "indications which identify a good as originating in the territory of a Member, or a region or locality in that territory, where a given quality, reputation or other characteristic of the good is essentially attributable to its geographical origin." The Administration expects that this definition will be applied in the context of trademark registration and that a "geographical indication" as used in this provision will be interpreted to comprise only those areas which have a reputation for being associated with the specific goods at issue. Obscure areas or those that do not have a reputation or other characteristics generally associated with wines or spirits should not be prohibited from registration.

f. Treatment of Inventive Activity

Section 531(a) of the implementing bill amends section 104 of the Patent Act (35 U.S.C. 104). The amendment is necessary to conform to Article 27.1 of the TRIPs Agreement, which specifies that patents are to be available without discrimination as to the place of invention. These changes will permit a patent applicant or patentee to establish a date of invention only for the purposes of obtaining an invention by using evidence of inventive activity that occurs in any WTO member country.

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The ability of an inventor to establish a date of invention can be a crucial factor affecting whether the inventor can obtain patent protection in the United States. For instance, if two or more parties independently develop and seek patent protection for the same invention, the patent will be granted to the party that can establish the earlier date of invention. Under current law, no evidence can be introduced by a party seeking to prove a date of invention if the evidence is based on activity that took place outside of the United States, Canada, or Mexico. The amendment to section 104(a)(1) will remove this restriction with respect to inventive activity that occurs within WTO member countries.

The implementing bill does not change present practice regarding the effect of a determination that establishes which of two or more inventors was the first inventor. This practice precludes the losing party from separately patenting the invention in dispute, even if the invention of the winning party was not made "in this country", pursuant to application of section 102(g) of Title 35, U.S. Code. Thus, a losing party is and will continue to be

precluded through interference estoppel from separately patenting the invention in dispute or an invention that is not patently distinguishable from the invention in dispute (see *In re Deckler*, 24 U.S.P.Q.3d 1448 (Fed. Cir. 1992)).

As foreign inventive activity may now be considered in a determination of which inventor was the first to invent, fairness to both U.S. and foreign inventors demands a certain identity of treatment with regard to reliance on inventive activity in the United States and abroad. Consequently, the inability of an inventor to rely on a date of invention in the United States where the invention has been subsequently abandoned, suppressed or concealed the invention under patentability determinations under Section 102(g) should apply equally to the inventor relying on foreign inventive activity.

Section 531(a) extends existing safeguards in section 104 of Title 35 to ensure fairness to U.S. inventors. Under the current section 104(a)(3), which was added by the NAFTA Implementation Act, when a party in a proceeding before the Patent and Trademark Office, a court, or another competent authority requests information in Mexico or Canada relevant to the date of invention by an opposing party, and the information is not made available to the same extent as it could be made available in the United States, the adjudicative body must "draw appropriate inferences" or take other action permitted by statute, rule, or regulation in favor of the party that requested but could not obtain the information. The implementing bill makes this provision applicable to information in any WTO member country.

Section 531(a) also extends section 104(a)(2) to address inventive activity by individuals in government service, where the activity takes place outside their home country. Under current law, an individual in government service can rely on evidence of inventive activity outside the United States to prove a date of invention. This privilege was extended to domiciliaries of NAFTA members by the NAFTA Implementation Act. The implementing bill extends this privilege to domiciliaries of any WTO member country.

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Section 531(b) addresses the effective date of the changes to section 104. This section specifies that the changes to section 104 will apply to all patent applications filed on or later than one year after the entry into force of the WTO Agreement with respect to the United States. The provision also specifies that an applicant for patent or a patentee may not establish a date of invention that is earlier than one year after the entry into force of the WTO Agreement with respect to the United States by reference to knowledge, use or activity in a WTO country other than provided in sections 119 and 365 of Title 35.

g. Term of Patent Protection; Domestic Priority System; Provisional Applications

Under present law, the term of a U.S. patent lasts 17 years from the date of its grant, provided the required fees for maintaining the patent in force are paid. Article 33 of the Agreement requires WTO member countries to provide a patent term of at least 20 years, measured from the date the application for patent was filed.

Section 532(a) of the bill changes the manner in which the term of a U.S. patent is measured. It amends section 154 of Title 35 to provide that the term of a patent will commence on the date of issue, and end twenty years after the date on which the application resulting in the patent was filed. If priority to an earlier application or applications is claimed under sections 120, 121, or 365(c) of Title 35, the 20-year period is measured from the date of the earliest of such applications. The term of a patent that results from any application that is filed on or after the date that is six months after the effective date of this Act shall end twenty years after the date said application was filed, or if priority to an earlier application or applications is claimed under sections 120, 121 or 365(c) of Title 35, 20 years from the date of the earliest of such applications.

Section 532(a) further amends section 154 of Title 35 to provide that priority under sections 119, 365(a), or 365(b) of Title 35 is not to be taken into account in

determining the term of a patent. This provision is necessary to comply with the requirements of Article 4 *bis*(5) of the *Paris Convention for the Protection of Industrial Property* under which countries must exclude from their measurement of patent term any periods for which an applicant has based a claim of priority to an earlier foreign-filed application.

Section 532(a) also amends section 154 of Title 35 to provide for extension of the term of patents for up to a total of five years under certain circumstances. These circumstances include delays caused by interference proceedings under section 135(a), by the imposition of secrecy orders under section 181, or when a patent is issued after an adverse determination of patentability has been reversed on appeal by either the Board of Patent Appeals and Interferences or a federal court.

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In calculating the period of time of the extension of term of a patent due to an interference proceeding, the Patent and Trademark Office will include time attributable to proceedings before the Board of Patent Appeals and Interferences, as well as time before a federal court. In calculating the period of time of the extension of term under section 154(b)(2) for an appeal, section 154(b)(3)(A) directs the Patent and Trademark Office to rely on the date an appeal was taken under section 134 or 141, or an action was commenced under section 145, whichever occurs first.

The length of a patent term extension provided under the authority of section 154(b)(2) may be reduced in two instances. First, the period of patent term extension for appeal will be reduced, pursuant to section 154(b)(3)(B), for periods of time attributable to appellate review before the expiration of three years from the filing date of the application leading to the patent. Second, under section 154(b)(3)(C), an extension will be reduced for time attributable to periods during which the applicant did not act with due diligence. Although extensions under section 154(b) are limited to a total of five years, patentees will continue to be able to obtain extensions of patent term for up to five years to compensate for delays caused by pre-marketing regulatory review under the authority of existing section 156 of title 35.

A further change in U.S. law incident to the change in how patent term is measured is required by virtue of the operation of Articles 33, 70.2 and 70.4 of the TRIPs agreement. Specifically, section 532(a) of the implementing bill amends section 154 to provide that the term of a patent in force on, or that results from an application filed before, the date that is six months after the date of enactment of the Uruguay Round Agreement Act will be the greater of 17 years from the date of patent grant or 20 years from the date of filing of the application leading to the patent. A patent whose term has been disclaimed under section 253 of Title 35 due to another patent on an invention that is not patentably distinct from but was owned by or subject to an obligation of assignment to the same person shall expire on the date of the other patent. A patent whose term has been disclaimed under section 253 of Title 35 independent of another patent shall be reduced by the length of the originally disclaimed period.

Section 532(a) also adds sections 154(c)(2) and (3). These sections address situations where a third party begins use of a patented invention before the date that is six months after the date of enactment of the Uruguay Round Agreements Act and such use becomes infringing because of a change in patent term due to operation of section 154(c)(1). In such circumstances, the patent owner will not be able to obtain an injunction, recover a reasonable royalty, or obtain attorneys fees as provided for in sections 283 to 285 of Title 35, but will be able to recover equitable remuneration from a third party who infringes the patent during the period in question.

Section 532(b)(1) of the bill amends section 119 of title 35 to establish a domestic priority system. Claims to domestic priority will be made possible through use of the provisional application system established by section 532(b)(3) of the bill. Provision of a

domestic priority right is important to ensure that applicants who file originally in the United States are not placed at a disadvantage in relation to applicants who file originally in foreign countries. As noted above, the Paris Convention precludes the United States from including in the measurement of patent term any period of time attributable to a claim for priority under 119, 365(a), or 365(b) of Title 35. The new section 119(e) extends this right to applicants that file in the United States a provisional application under section 111(b) of title 35. This will provide applicants who take advantage of this section a period of up to 12 months in which to file the formal application but claim priority based on the provisional application filed in the United States, which period will not be included in the calculation of patent term.

Section 532(b)(3) amends section 111 of title 35 to establish a provisional application system. Section 111(b) will permit an applicant to file a simplified "provisional" application for a fee of $150, or $75 for small entities, that can serve as a basis for a claim of priority if the applicant subsequently files a formal patent application within 12 months of the filing of the provisional application. The provisional application must contain a specification and any necessary drawings, in compliance with 35 U.S.C. 112 and 113, and the applicant must pay the required fee, in order to obtain a filing date for the provisional application. The provisional application need not include claims. The provisional application will not be examined, and will expire twelve months after it was filed. The inventor must present an application in compliance with all statutory requirements in order to begin the patent examination process; a provisional application cannot mature into a patent. The new section 111(b)(6) explicitly permits an applicant that has filed an application in full compliance with section 111(a) to treat said application as a provisional application under section 111(b).

Finally, section 532(c) makes conforming changes to sections 156, 172, 173, 365, and 373 of Title 35.

h. Extending the Definition of Infringing Activity

Article 28 of the Agreement sets out the rights that WTO member countries must provide through the grant of a patent. Under Article 28.1, a product patent must confer on its owner the right to prevent others from making, using, offering for sale, selling, or importing the protected invention. Under Article 28.1, a process patent must confer on its owner the right to prevent others from using the process, and from using, offering for sale, selling, or importing the product obtained directly from the process.

Under current law, a patent in the United States provides its holder the right to exclude others from making, using, or selling the invention in the United States, and to prevent importation of a product produced outside the United States using a process subject to a U.S. patent. Section 533 of the bill amends section 154 of title 35 to conform to the requirements of Article 28. This section adds to the current rights provided by section 154 the right to preclude others from offering for sale or importing a product covered by a

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United States patent. In addition, it enables the holder of a U.S. process patent to prevent others from offering to sell the products made by the patented process. Section 533 of the bill also makes appropriate conforming changes to sections 41(c)(2), 252, 262, 271, 272, 287, 292, 295 and 307 of Title 35.

2. <u>Administrative Action</u>

a. Compulsory Licensing

Article 31 of the Agreement on TRIPs limits the extent to which WTO member countries may grant "compulsory licenses," that is, permit the use by the government or third parties of a patented product or process without the patent owner's

permission. The article sets out a number of conditions a government must meet before granting such a license.

U.S. law currently provides for the issuance of compulsory licenses under three statutes -- the Atomic Energy Act, the Clean Air Act, and the Energy Policy Act (which amended the Atomic Energy Act). Regulations governing the grant of compulsory licenses under each of these statutes currently require satisfaction of all of the conditions set out in Article 31 except the requirement in paragraph (c), which specifies that compulsory licenses on semiconductor technology may be granted only for a public non-commercial use or to remedy an anticompetitive practice.

The Department of Energy will modify regulations set out at 10 CFR Part 780, and the Environmental Protection Agency will amend its regulations implementing section 308 of the Clean Air Act, to meet the requirements of Article 31(c) for any compulsory licenses they issue in respect of semiconductor technology or designs. In addition, the President will issue an Executive Order ensuring that all government agencies that may invoke "government use" provisions meet those requirements as well.

b. Patent Applications

To facilitate the completion of prosecution of applications pending in the Patent and Trademark Office as of the effective date of section 154(a)(2), section 532(a)(2) directs the Commissioner of Patents and Trademarks to establish regulations for two purposes.

The first purpose is to provide for further limited reexamination of an application pending for two years or longer as of the effective date of section 154(a)(2) of title 35, taking into account any reference made in such application to any earlier filed application under sections 120, 121 or 365(c) of title 35. The further limited reexamination will permit applicants to present for consideration a submission after the Patent and Trademark Office has issued a final rejection on an application.

[page 1006]

The types of submissions shall include, but shall not be limited to, an information disclosure statement, an amendment to the specification or claims, or new substantive arguments or new evidence in support of patentability of the claimed invention. The Patent and Trademark Office will consider on the merits the first and second such submissions, to the extent that such submissions would have been entitled to consideration if made prior to final rejection. The Patent and Trademark Office will modify such final rejection or allow such application, as appropriate, based on the consideration of such submissions. As is current practice, the Patent and Trademark Office shall consider any submission which, in the opinion of the Patent and Trademark Office, places the application in condition for allowance or in better condition for appeal. The Commissioner will determine an appropriate fee, related to the reexamination provided, for the filing of such submissions.

The second purpose for the new regulations is to address Patent and Trademark Office restriction requirements and filings of divisional applications, and to ensure that there is an opportunity for an applicant to respond to a requirement for restriction or for the filing of a divisional application. After the effective date of section 154(a)(2), the Patent and Trademark Office will not make or maintain a requirement for restriction or the filing of a divisional application for an application that has been pending for three years or longer as of the effective date of said section, taking into account any reference made in such application to any earlier filed application under sections 120, 121 or 365(c) of title 35. This limitation does not apply if such a requirement was first made in such application or a predecessor application more than two months prior to such effective date, or if there has not been at least one Patent and Trademark Office action due to actions by the applicant. The Commissioner will determine an appropriate fee for examination of each independent and distinct invention in an application in excess of one.

Measuring the term of a patent from the filing date of the patent application instead of from the date of grant of the patent increases the importance of expeditious processing of applications by the Patent and Trademark Office. The Administration continues to be committed to working with the Congress to ensure that adequate resources are available for prompt processing of all patent applications. The Patent and Trademark Office will continue its efforts to hire and retain sufficient numbers of highly qualified examiners to enable it to handle the increasing number of applications being filed in complex technological areas, such as biotechnology, computers, and software. The Patent and Trademark Office will also continue its efforts to provide adequate legal and technical training for its examiners to ensure that the patent examining corps is equipped to handle increasingly complex patent applications expeditiously.

Some in industry have expressed concerns over possible sources of delay during examination of patents that could lead to a decrease in effective patent term. Such concerns focus on the Office's application of the utility requirement during examination of patent applications claiming pharmaceutical inventions. Under U.S. law, if a patent application contains a disclosure of utility that corresponds in scope to the subject matter

sought to be patented, the specification must be taken as sufficient to satisfy the utility requirement of section 101 of title 35 for the entire claimed subject matter, unless there is reason for one skilled in the art to question the objective truth of the statement of utility or its scope. If the Office rejects an application on the grounds that the invention lacks utility, the applicant may provide evidence supporting the truth of the statement of utility and its scope as found in the specification. If the evidence is persuasive, a rejection for lack of utility may be overcome. An applicant may satisfy the utility requirement for a pharmaceutical invention by demonstrating evidence of pharmacological activity in either *in vitro* or *in vivo* experiments such that a person skilled in that field would conclude that utility has been established. Under most circumstances, human clinical data is not necessary to establish utility. And, to ensure that concerns related to utility are fully addressed, the Patent and Trademark Office will sponsor a public hearing to ascertain whether patentees claiming protection for biotechnological inventions lose effective patent term in the course of developing evidence to establish that such inventions are in fact useful.

c. Geographical Indications

The United States will implement the Agreement's provisions on geographical indications for wine and spirits through the labeling regulations of the Bureau of Alcohol, Tobacco and Firearms of the Department of the Treasury. The Agreement specifically recognizes that rights in geographic indications for wine and spirits may be enforced through administrative action.

d. Border Enforcement

The Agreement on TRIPs contains detailed provisions on border enforcement against imports of pirated and counterfeit goods. Although U.S. law and customs regulations already meet the minimum TRIPs requirements, current customs regulations do not provide for uniform procedures in the treatment of copyright and trademark infringement actions. The Customs Service will issue revised regulations to harmonize those requirements.

EXHIBIT I

(7) URUGUAY ROUND AGREEMENTS.—The term "Uruguay Round Agreements" means the agreements approved by the Congress under section 101(a)(1).

(8) WORLD TRADE ORGANIZATION AND WTO.—The terms "World Trade Organization" and "WTO" mean the organization established pursuant to the WTO Agreement.

(9) WTO AGREEMENT.—The term "WTO Agreement" means the Agreement Establishing the World Trade Organization entered into on April 15, 1994.

(10) WTO MEMBER AND WTO MEMBER COUNTRY.—The terms "WTO member" and "WTO member country" mean a state, or separate customs territory (within the meaning of Article XII of the WTO Agreement), with respect to which the United States applies the WTO Agreement.

TITLE I—APPROVAL OF, AND GENERAL PROVISIONS RELATING TO, THE URUGUAY ROUND AGREEMENTS

Subtitle A—Approval of Agreements and Related Provisions

19 USC 3511.

SEC. 101. APPROVAL AND ENTRY INTO FORCE OF THE URUGUAY ROUND AGREEMENTS.

(a) APPROVAL OF AGREEMENTS AND STATEMENT OF ADMINISTRATIVE ACTION.—Pursuant to section 1103 of the Omnibus Trade and Competitiveness Act of 1988 (19 U.S.C. 2903) and section 151 of the Trade Act of 1974 (19 U.S.C. 2191), the Congress approves—

(1) the trade agreements described in subsection (d) resulting from the Uruguay Round of multilateral trade negotiations under the auspices of the General Agreement on Tariffs and Trade, entered into on April 15, 1994, and submitted to the Congress on September 27, 1994; and

(2) the statement of administrative action proposed to implement the agreements that was submitted to the Congress on September 27, 1994.

(b) ENTRY INTO FORCE.—At such time as the President determines that a sufficient number of foreign countries are accepting the obligations of the Uruguay Round Agreements, in accordance with article XIV of the WTO Agreement, to ensure the effective operation of, and adequate benefits for the United States under, those Agreements, the President may accept the Uruguay Round Agreements and implement article VIII of the WTO Agreement.

(c) AUTHORIZATION OF APPROPRIATIONS.—There are authorized to be appropriated annually such sums as may be necessary for the payment by the United States of its share of the expenses of the WTO.

(d) TRADE AGREEMENTS TO WHICH THIS ACT APPLIES.—Subsection (a) applies to the WTO Agreement and to the following agreements annexed to that Agreement:

(1) The General Agreement on Tariffs and Trade 1994.

(2) The Agreement on Agriculture.

EXHIBIT J

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO.: 4,626,538

DATED: December 2, 1986

INVENTOR(S): Dusza et al.

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

On the face of the patent, cancel at [*] Notice: "The portion of the term of this patent subsequent to Jun. 3, 2002, has been disclaimed."

and substitute

The portion of the term of this patent subsequent to the expiration date of U.S. Patent No. 4,521,422 has been disclaimed.

Mailing Address of Sender:

Finnegan, Henderson, Farabow
Garrett & Dunner, L.L.P.
1300 I Street, N.W.
Washington, DC 20005-3315

PATENT NO. 4,626,538

No. of add'l copies
@ 50¢ per page

⇒ _____

FORM PTO 1050 (Rev.2-93)

EXHIBIT K

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
ASSISTANT SECRETARY AND COMMISSIONER
OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

Paper No. 25

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SPECIAL PROGRAMS OFFICE
DAC FOR PATENTS

THOMAS SARRO
LARSON AND TAYLOR
SUITE 900
1199 NORTH FAIRFAX STREET
ALEXANDRIA, VIRGINIA 22314

In re Patent No: 4,346,116 :
Application No. 06/151,816 :
Filed: October 31, 1984 : DECISION DENYING PETITION
Issue date: August 24, 1982 :
Inventor: Francoise Verwaerde et al :

This is a decision on the renewed petition under 37 CFR 1.182, which now requests that the PTO "give notice to the public of the true expiration date of the patent, i.e., May 14, 1999."

The petition is DENIED.

BACKGROUND

In response to the final Office action of August 19, 1991 , wherein the examiner rejected inter alia, various claims over claims 6 and 7 of copending application No. 038,711, applicants filed an amendment and a terminal disclaimer on December 21, 1981. The accompanying remarks noted:

> "[t]he amendment (sic, rejection) of claims 27-34 and 37-40 as obvious variants of claims in Serial No. 038,711 is being obviated by the Terminal Disclaimer submitted herewith."

The application was allowed by the examiner in the Office communication mailed March 15, 1992, and issued August 24, 1982.

A petition filed September 11, 1997, requested under 37 CFR 1.182 that the recorded terminal disclaimer filed on December 21, 1981, be withdrawn in favor of a revised, apparently forthcoming, terminal disclaimer, and further, that a Certificate of Correction (PTO mistake) be issued to that effect. Petitioners specifically requested that the aforementioned original terminal disclaimer be replaced, in that the instant patent term, via the original terminal disclaimer, is limited to the pre "GATT-NAFTA" (Uruguay

Round Agreements Act (URAA) (1994)) expiration date for U.S. Patent No. 4,279,931 (July 21, 1998), while the latter patent now expires May 14, 1999, as was apparently to be reflected in any forthcoming terminal disclaimer. As such, petitioner asserted, the instant patent contains an erroneous date of expiration, and further, as the error in the patent is not the fault of petitioner, no fees for either the petition, or the requested Certificate of Correction, should be assessed.

The petition was dismissed in the decision of February 11, 1998.

The instant renewed petition was filed April 13, 1998.

STATUTE AND REGULATION

35 USC § 253 states that:

> Whenever, without any deceptive intention, a claim of a patent is invalid the remaining claims shall not thereby be rendered invalid. A patentee, whether of the whole or any sectional interest therein, may, on payment of the fee required by law, make disclaimer of any complete claim, stating therein the extent of his interest in such patent. disclaimer shall be in writing, and recorded in the Patent and Trademark Office; and it shall thereafter be considered as part of the original patent to the extent of the interest possessed by the disclaimant and by those claiming under him.
>
> In like manner any patentee or applicant may disclaim or dedicate to the public the entire term, or any terminal part of the term, of the patent granted or to be granted.

35 USC § 254 provides:

> Whenever a mistake in a patent, incurred through the fault of the Patent and Trademark Office, is clearly disclosed by the records of the Office, the Commissioner may issue a certificate of correction stating the fact and nature of such mistake, under seal, without charge, to be recorded in the records of patents. A printed copy thereof shall be attached to each printed copy of the patent, and such certificate shall be considered as part of the original patent. Every such patent, together with such certificate, shall have the same effect and operation in law on the trial of actions for causes thereafter arising as if the same had been originally issued in such corrected form. The Commissioner may issue a

corrected patent without charge in lieu of and with like effect as a certificate of correction.

35 USC § 255 states that:

> Whenever a mistake of a clerical or typographical nature, or of minor character, which was not the fault of the Patent and Trademark Office, appears in a patent and a showing has been made that such mistake occurred in good faith, the Commissioner may, upon payment of the required fee, issue a certificate of correction, if the correction does not involve such changes in the patent as would constitute new matter or would require re-examination. Such patent, together with the certificate, shall have the same effect and operation in law on the trial of actions for causes thereafter arising as if the same had been originally issued in such corrected form.

37 CFR 1.182 provides that:

> All situations not specifically provided for in the regulations of this part will be decided in accordance with the merits of each situation by or under the authority of the Commissioner, subject to such other requirements as may be imposed, and such decision will be communicated to the interested parties in writing. Any petition seeking a decision under this section must be accompanied by the petition fee set forth in § 1.17(h).

37 CFR 1.322 provides that:

> (a) A certificate of correction under 35 U.S.C. 254 may be issued at the request of the patentee or the patentee's assignee. Such certificate will not be issued at the request or suggestion of anyone not owning an interest in the patent, nor on motion of the Office, without first notifying the patentee (including any assignee of record) and affording the patentee an opportunity to be heard. When the request relates to a patent involved in an interference, the request shall comply with the requirements of this section and shall be accompanied by a motion under § 1.635.
>
> (b) If the nature of the mistake on the part of the Office is such that a certificate of correction is deemed inappropriate in form, the Commissioner may issue a corrected patent in

lieu thereof as a more appropriate form for certificate of correction, without expense to the patentee.

37 CFR 1.321 states:

(a) A patentee owning the whole or any sectional interest in a patent may disclaim any complete claim or claims in a patent. In like manner any patentee may disclaim or dedicate to the public the entire term, or any terminal part of the term, of the patent granted. Such disclaimer is binding upon the grantee and its successors or assigns. A notice of the disclaimer is published in the Official Gazette and attached to the printed copies of the specification. The disclaimer, to be recorded in the Patent and Trademark Office, must:

(1) be signed by the patentee, or an attorney or agent of record;

(2) identify the patent and complete claim or claims, or term being disclaimed. A disclaimer which is not a disclaimer of a complete claim or claims, or term, will be refused recordation;

(3) state the present extent of patentee's ownership interest in the patent; and

(4) be accompanied by the fee set forth in § 1.20(d).

(b) An applicant or assignee may disclaim or dedicate to the public the entire term, or any terminal part of the term, of a patent to be granted. Such terminal disclaimer is binding upon the grantee and its successors or assigns. The terminal disclaimer, to be recorded in the Patent and Trademark Office, must:

(1) be signed:

(i) by the applicant, or

(ii) if there is an assignee of record of an undivided part interest, by the applicant and such assignee, or

(iii) if there is an assignee of record of the entire interest, by such assignee, or

(iv) by an attorney or agent of record;

(2) specify the portion of the term of the patent being disclaimed;

(3) state the present extent of applicant's or assignee's ownership interest in the patent to be granted; and

(4) be accompanied by the fee set forth in § 1.20(d).

(c) A terminal disclaimer, when filed to obviate a judicially created double patenting rejection in a patent application or in a reexamination proceeding, must:

(1) Comply with the provisions of paragraphs (b)(2) through (b)(4) of this section;

(2) Be signed in accordance with paragraph (b)(1) of this section if filed in a patent application or in accordance with paragraph (a)(1) of this section if filed in a reexamination proceeding; and

(3) Include a provision that any patent granted on that application or any patent subject to the reexamination proceeding shall be enforceable only for and during such period that said patent is commonly owned with the application or patent which formed the basis for the rejection.

(c) A terminal disclaimer, when filed to obviate a judicially created double patenting rejection in a patent application or in a reexamination proceeding, must:

(1) Comply with the provisions of paragraphs (b)(2) through (b)(4) of this section;

(2) Be signed in accordance with paragraph (b)(1) of this section if filed in a patent application or in accordance with paragraph (a)(1) of this section if filed in a reexamination proceeding; and

(3) Include a provision that any patent granted on that application or any patent subject to the reexamination proceeding shall be enforceable only for and during such period that said patent is commonly owned with the application or patent which formed the basis for the rejection.

37 CFR 1.323 states that:

> Whenever a mistake of a clerical or typographical nature or of minor character which was not the fault of the Office, appears in a patent and a showing is made that such mistake occurred in good faith, the Commissioner may, upon payment of the fee set forth in § 1.20(a), issue a certificate, if the correction does not involve such changes in the patent as would constitute new matter or would require reexamination. A for a certificate of correction of a patent involved in an interference shall comply with the requirements of this section and shall be accompanied by a motion under § 1.635.

OPINION

Petitioners request reconsideration in that the decision of February 11, 1998 is asserted to have failed to address the basis of the prior request filed September 11, 1997. Specifically petitioners assert, the Commissioner has authority under 37 CFR 1.182 to give notice to the public of the true expiration date of the above-captioned patent, which petitioner contends, is May 14, 1999.

The showing of record fails to adequately demonstrate that the facts of this case warrant the relief(s) requested.

The terminal disclaimer under 35 USC § 253 and 37 CFR 1.321, filed December 21, 1981, was relied upon by petitioners to overcome a rejection on the grounds of obviousness type double patenting involving the claims of commonly owned U. S. Patent No. 4,279,931 issued July 21, 1981. The terminal disclaimer was executed by Germain Roquette, on behalf of the assignee, Roquette Freres, and specified in pertinent part that:

> "The said assignee does hereby disclaim and dedicate to the public the terminal portion of any United States Patent to be issued on this application beyond July 21, 1998."

While petitioners now predicate their request for withdrawal of the recorded terminal disclaimer upon a subsequent change in the term of the '931 patent, inspection of the above-quoted language in that disclaimer reveals that petitioners originally made such disclaimer contingent upon an actual date of expiration of the term of the '931 patent. That is, petitioners made the original terminal disclaimer absolute, that is, date-specific to July 21, 1998. It follows that regardless of what effect the URAA may have

subsequently had on the expiration date of the '931 patent, there is no nexus between that date and the specific expiration date as set forth in the original terminal disclaimer of record. As such, no error is apparent in the term of the original instant letters patent, as indicated by the recorded terminal disclaimer, which warrants correction. As such, it is not apparent from the record, and petitioner has not shown, on the record, how the express date certain patent expiration of July 21, 1998 given by the assignee of the entire interest, becomes May 14, 1999. Rather, as the patent was freely stated to expire on July 21, 1998 whatever effects the URAA might have had on the term of other patent, is simply immaterial to the date specific expiration of the above-captioned patent. Contrary to petitioners' contention, whatever authority may be vested under and by the patent statutes and rules of practice, such authority does not controvert the assignee's express statement of a date certain expiration of the instant patent. In other words, it is manifestly inconsistent with the express language supplied by petitioners in the above-noted terminal disclaimer to now aver that the "true expiration date" is any other than that specifically recited in the terminal disclaimer, and proclaimed to the public as part of the instant patent since its date of issuance.

It is also brought to petitioners' attention that:

> "The purpose of the URAA [codified in part in 35 U.S.C. § 154] **was not to extend patent terms**, although it has that effect in some cases, but to harmonize the term provision of United States patent law with that of our leading trading partners which grant a patent term of 20 years from the date of filing of the patent application. Prior to June 8, 1995, U.S. patents had an expiration date under 35 U.S.C. Section 154 **measured as 17 years from the date the patent issued, except where terminal disclaimers were filed.** Amended section 154(a) now reads:
>
> > Subject to the payment of fees under this title, such grant shall be for a term beginning on the date on which the patent issues and ending 20 years from the date on which the application for the patent was filed in the United States or, if the application contains a specific reference to an earlier filed application or applications under section 120, 121, or 365(c) of this title, from the date on which the earliest such application was filed.

35 U.S.C. § 154(a)(2) (1994).

For certain patents which were issued and for pending applications which were filed prior to June 8, 1995, a transitional provision preserves a guaranteed 17-year term, if it is longer than 20 years from filing, by the following provision:

> The term of a patent that is in force on or that results from an application filed before the date that is 6 months after the date of the enactment of the Uruguay Round Agreements Act **shall be the greater of the 20-year term as provided in subsection (1), or 17 years from grant, subject to any terminal disclaimers.**

> Id. at Section 154(c)(1). Patents in the section 154(c)(1) category thus are entitled to keep or to enjoy the 17-year term from issuance of the patent or a 20-year from filing term, whichever is longer."[1] (emphasis added)

The statutory authority for amendment or correction of an issued patent is found in title 35, chapter 25. The instant petition does not involve correction of a mistake by the Patent and Trademark Office (Office) (35 USC § 254) or correction of the named inventor (35 USC § 256). In addition, while the instant petition involves a disclaimer, 35 USC § 253 merely authorizes the filing and recording of disclaimers; it does not authorize the withdrawal of a terminal disclaimer. Finally, petitioners have not sought amendment or correction by reissue (35 USC §§ 251 and 252).

Unless a "mistake" is provided for in 37 CFR 1.322, 1.323, or 1.324, or affords legal grounds for reissue or for reexamination, such "mistake" will not be corrected subsequent to the issuance of an application as a patent. See 37 CFR 1.325. As stated in section 1490 of the Manual of Patent Examining Procedure (MPEP) (6th Ed., Rev. 3 1997), the mechanisms to correct a patent (i.e., certificate of correction (35 USC § 255), reissue (35 USC § 251) and reexamination (35 USC § 305)) are not available to withdraw or otherwise nullify the effect of a recorded terminal disclaimer.

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[1] Merck & Co. v. Kessler, 80 F.3d 1543, 1547-1548, 38 USPQ2d 1347, 1349-1350 (Fed. Cir. 1996).

Further in this regard, the public has had fifteen (fifteen) years since the grant of the above-identified patent, to act on its facial representation that the term of this patent will expire, at the latest, on July 21, 1998. Similarly, petitioners have had, since the submission of the aforementioned terminal disclaimer on December 21, 1981, no reasonable basis to expect a term for this patent that would extend beyond July 21, 1998.

While petitioners may now consider the originally filed disclaimer to be unnecessary, or unnecessarily limiting, petitioners are, nevertheless, confronted with what has been characterized as "an unhappy circumstance", rather than a circumstance necessitating relief. See In re Jentoft, 392 F.2d 633, 639 n. 6, 157 USPQ 363, 368 n. 6 (CCPA 1968); MPEP 1490. When the question of whether or not a given set of claims in one application or patent is distinct from another set of claims in another application or patent with respect to obviousness double patenting arises, that question relates to the merits of an invention, and the appropriate remedy for resolution of that issue ultimately lies by appeal as provided by statute. See e.g. In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Petitioners had the opportunity to challenge the need for a terminal disclaimer, on appeal, but instead, freely chose to file a terminal disclaimer to avoid the rejection, during the prosecution of the application that led to the above-identified patent. Such does not afford proper legal or public policy grounds for requesting nullification of the terms of free dedication to the public contained in the previously filed terminal disclaimer by way of appeal, much less on petition. Cf. Ex Parte Anthony, 230 USPQ 467 (PBAI 1982) aff'd. No. 84-1357 (Fed. Cir. June 14, 1985).

Even assuming, *arguendo*, the relief(s) requested should be considered on petition, petitioners are reminded that, as a general rule, public policy does not favor the restoration to the patentee [applicant] of something that has been freely dedicated to the public, particularly where the public interest is not protected in some manner, e.g., intervening rights in the case of a reissue patent. See Altoona Publix Theatres v. American Tri-Ergon Corp., 294 U.S. 477, 24 USPQ 308 (1935). Petitioners have failed to provide a reasonable, much less any, assurance that the public interest will, or can be, protected if the relief(s) requested in this petition are given favorable consideration. In this regard, an applicant's use, and Office acceptance, of a terminal disclaimer is in the public interest because such encourages the disclosure of additional developments, the earlier filing of patent applications, and the earlier expiration of

patents whereby the inventions covered become freely available to the public. Jentoft, supra. It is brought to petitioners' attention that the principle against recapturing something that has been intentionally dedicated to the public dates back at least to Leggett v. Avery, 101 U.S. 246 (1879). As noted above, while petitioners may now consider the previously filed disclaimer to be unnecessary, or unnecessarily limiting, petitioners are, nevertheless, confronted with what has been characterized as "an unhappy circumstance", rather than a circumstance(s) necessitating relief. Jentoft at 639 n. 6, 157 USPQ at 368 n. 6.

Moreover, petitioners have made no attempt to explain their delay in presenting this petition, over two years after the implementation of the URAA. The public has thus had some two years within which to rely on the fact that, notwithstanding the URAA of 1994, and its effective date of June 8, 1995, petitioners permitted the original terminal disclaimer in this patent to continue in unabated force and effect. While petitioners should not infer that, had the instant petition been more seasonably presented, a different result might have been obtained; nevertheless, the record shows that petitioners did not diligently address the issues pertaining to the instant terminal disclaimer presented by the aforementioned URAA. Assuming, *arguendo*, that petitioners may, seasonably or otherwise, request rescission of the terminal disclaimer of record, equitable powers should not be invoked to excuse the performance of a condition by a party that has not acted with reasonable, due care and diligence. U.S. v. Lockheed Petroleum Services, 709 F.2d 1472, 1475 (Fed. Cir. 1983).

In any event, to withdraw the recorded terminal disclaimer filed on December 21, 1981 and properly recorded in the above-identified patent, such action must be authorized pursuant to 35 USC § 255.

A Certificate of Correction under 35 USC § 255 and 37 CFR 1.323 is available for the correction of errors of a minor or clerical character, and does not extend to the correction of errors that would constitute new matter or would require reexamination. See In re Arnott, 19 USPQ2d 1049, 1054 (Comm'r Pat. 1991); In re Hyman, 185 USPQ 441, 442 (Sol. Pat. 1975). Specifically, 35 USC § 255 requires, *inter alia*, that two specific and separate requirements be met prior to the issuance of a Certificate of Correction. The first requirement is that the mistake is: (1) of a clerical nature, (2) of a typographical nature, or (3) of minor character. The second requirement is that the correction must not involve changes that would: (1) constitute new matter or (2) would

require reexamination. See Arnott 19 USPQ2d at 1052; see also MPEP 1490.

Apparently, the "mistake" at issue here involves petitioners' inclusion in the terminal disclaimer filed December 21, 1981, of a specific expiration date: July 21, 1998. However, this "mistake" is not one of a clerical or typographical nature; rather correcting this "mistake" would involve a substantive change to the recorded terminal disclaimer of record. Secondly, the "broadening" of the claims of a patent, via the attempted removal of a recorded terminal disclaimer, requires reexamination (pursuant to 35 USC § 251) of the issues raised thereby. See Anthony, supra. Further, in this regard, even while 35 USC 251 is a remedial statute, and, as such, is often liberally construed, nevertheless, there is a two year bar on any remedy that would effectuate broadening of an issued patent. See 35 USC 251. As held in Anthony, however, removal of a recorded terminal disclaimer, and the resultant "broadening" of the vertical scope (term) of the original patent, is prohibited, *inter alia*, if the attempt via reissue is not sought within two years of the patent grant. See id. at 470. It would appear to be an improper exercise of 37 CFR 1.182 to permit petitioner to regain, on petition, what petitioner could not herein regain under the remedial patent statute, which, as such, is "liberally construed." Under the facts of this case, it would be an inappropriate exercise of 37 CFR 1.182 to rescind the terminal disclaimer.

DECISION

For the reasons given above, it would be an inappropriate exercise of 37 CFR 1.182 to rescind the terminal disclaimer of record. Accordingly, the petition is granted to the extent that the previous decision has been reconsidered, but is **denied** as to rescinding the terminal disclaimer of record.

This patent file is being returned to the Files Repository.

Telephone inquiries relative to this decision should be directed to Special Projects Examiner Brian Hearn at (703) 305-1820.

Manuel A. Antonakas
Director, Office of Patent Policy Dissemination
Office of the Deputy Assistant Commissioner
for Patent Policy and Projects

EXHIBIT L

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
ASSISTANT SECRETARY AND COMMISSIONER
OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

Paper No. 24

KEIL & WEINKAUF
1101 CONNECTICUT AVENUE, N.W.
WASHINGTON, D.C. 20036

In re Patent No: 4,654,073 :
Application No. 06/666,908 :
Filed: October 31, 1984 : DECISION GRANTING PETITION
Issue date: March 31, 1987 :
Inventor: Dieter Jahn et al. :

This is a decision on the renewed petition filed March 9, 1998, under 37 CFR 1.182, that the recorded terminal disclaimer filed on March 14, 1986, be withdrawn in favor of the terminal disclaimer filed with the petition, and further, that a Certificate of Correction (PTO mistake) be issued to that effect.

The petition is granted to the extent indicated below.

Petitioner again requests that the aforementioned original terminal disclaimer be replaced with that filed August 27, 1997 in that the instant patent term, via the original terminal disclaimer, is limited to the pre "GATT-NAFTA" (i.e., the Uruguay Round Agreements Act (URAA) (1994)) expiration date for U.S. Patent No. 4,422,864 (December 27, 2000), while the latter patent now expires May 20, 2002, as reflected in the newly proffered terminal disclaimer. As such, petitioner asserts, the instant patent contains an erroneous date of expiration, and further, as the error in the patent is not the fault of petitioner, no fees for either the petition, or the requested Certificate of Correction, should be assessed.

The terminal disclaimer filed under 35 USC § 253 and 37 CFR 1.321(c) on March 14, 1986, was relied upon by petitioner to overcome a rejection on the grounds of obviousness-type double patenting involving the claims of commonly owned U. S. Patent No. 4,442,864. The terminal disclaimer was executed by Messrs. Raemisch and Richters, on behalf of the assignee, BASF Aktiengesellschaft, and specified in pertinent part that:

> "Your Petitioner, by two duly authorized representatives, hereby disclaims the terminal part of any patent granted on the above-identified application which would extend beyond the expiration date of United States Patent No. 4,422,864 **(expiration date December 27, 2000)**, which is also owned by petitioner...[emphasis added]"

At the time the instant patent was published, the PTO printed thereon the specific expiration date, i.e., December 27, 2000, of U.S. Patent No. 4,422,864 as the end of the term of the instant patent as such date was then identical to the "expiration date," notwithstanding petitioner's concurrent use of the relative term "the expiration date of United States Patent No. 4,422,864."

Due to the changes to 35 U.S.C. § 154(c)(1) contained in Public Law 103-465, § 532, 108 Stat. 4809 (1994), the expiration date of U.S. Patent No. 4,422,864 (as well as the instant patent) is not December 27, 2000; rather it is now May 20, 2002, as correctly noted by petitioner. Thus, the terminal disclaimer of March 14, 1986 creates an ambiguity, in that it sets forth two (2) dates beyond which the terminal date of the above-identified patent is disclaimed: December 27, 2000, and May 20, 2002.

However, in order to resolve the ambiguity in the aforementioned terminal disclaimer filed on March 14, 1986 created by the changes to 35 U.S.C. 154(c)(1) contained in Public Law 103-465, it is not necessary, as requested by petitioner, to substitute the proffered terminal disclaimer for that already recorded. Rather, the correction of the terminal disclaimer date indicated on a patent due to the changes to 35 U.S.C. § 154 contained in Public Law 103-465, § 532, 108 Stat. 4809 (1994) is, if such correction is appropriate, by way of 35 U.S.C. § 254 and 37 CFR 1.322. However, in light of possible future changes to the patent statutes, the proffered Certificate of Correction, as it also recites a specific expiration date, might tend to replicate the problem already encountered herein. As such, the proffered Certificate of Correction will not be accepted.

Nevertheless, the instant file is being forwarded to Certificates of Correction Branch for issuance of a Certificate of Correction to now indicate that, in lieu of the former statement pertaining to the expiration of the term by way of a terminal disclaimer :

--[*] Notice: This patent is subject to a terminal disclaimer.--

Telephone inquiries relative to this decision should be directed to the undersigned at (703) 305-1820.

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for Patent Policy and Projects